tremity be so completely involved when other entire extremities in the same individual have completely escaped? "It would seem that all of the anterior horn cells of an extremity are probably affected together, with the resulting paralysis depending on intrinsic factors, such as blood supply, pressure from edema, or activity" (*3*).

Localization of Paralysis

There have been many peculiar individual occurrences of localization of paralysis in poliomyelitis, each of which might be well explained as a coincidence, but all of which, when accumulated, can be explained by the common factor of alteration of circulation. A few examples follow:

In the *Journal of the American Medical Association* for 8 September 1945, Brown, Francis, and Pearson describe a peculiarly significant occurrence of poliomyelitis in a child 19 days after the virus of poliomyelitis was first isolated from his stools. Although this child was harboring the virus for 19 days (the usual incubation period is 7–14 days), he remained well until immediately after a canoe race in which his arms were used as paddles. That evening he developed paralysis only in his arms. To deny the significance of association between the canoe race and the development of paralysis in the arms, one would have to postulate two unusual simultaneous coincidences: (1) the onset of paralysis immediately after the canoe race in a child infected at least 19 days previously; (2) the limitation of paralysis to the extremities used, the arms (a relatively rare distribution of paralysis in poliomyelitis).

A recent case of poliomyelitis in Los Angeles developed his only paralysis in a leg which four months previously had had a compound fracture and in which a plate had been inserted to hold the femur. Obviously, such an accident and surgical procedure would alter the circulation of that extremity.

The writer in his personal experience has seen three individuals develop poliomyelitis within 14 days of an immunization procedure, with its usual subsequent localized edema and induration, residual paralysis remaining only in the extremity in which the inoculation occurred.

The peculiar localizing effects of definitely established trauma or overactivity on the paralysis in such cases force one to consider seriously the common factor of circulatory disturbance as a determining factor in the development of paralysis.

Recent attempts to explain the action of Sister Kenny's therapy have revealed that interference with the circulation of the cord of the dog causes damage to the internuncial cells similar to that seen in poliomyelitis.

Alteration of Spinal Cord Circulation in Poliomyelitis

We are attempting in Los Angeles to alter circulation of the spinal cord in animals and humans with poliomyelitis, with a view toward altering the course of the disease. The paravertebral block is one method being tried.

A successful paravertebral block will, of course, increase the circulation of an extremity. That the circulation of that part of the cord supplying that extremity is increased has not as yet been shown. We are, however, proceeding for the time being on the inference that the extremity and that part of the spinal cord supplying the extremity operate as a single physiological unit, and anything which alters the circulation of the extremity will also alter the circulation of the cord involved.

It should be clearly understood that this is merely a preliminary report of work going on, made with the hope that it will stimulate others to investigate this field. Our results are too inadequate to warrant any conclusion that paravertebral block is a treatment for poliomyelitis. We do feel, however, that similar studies to determine the effect of alteration of circulation on residual paralysis and muscle spasm are indicated by much evidence.

Conclusion

A careful analysis of the distribution of paralysis in 1,200 cases of poliomyelitis and localizing effects of trauma or strain points toward alteration of the circulation of the spinal cord as being a determining factor. The paravertebral block is being studied as one possible means of altering that circulation.

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The Effect of Thiouracil and Thyroactive Substances on Mouse Susceptibility to Poliomyelitis Virus[1]

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An investigation of the effect of environmental temperature on the resistance of Swiss white mice to poliomyelitis virus (*1*) suggested that the marked tolerance of these animals to the infectious agent, when acclimated to low temperatures, might be due to an altered metabolic rate of their tissues, inter-

[1] The writer wishes to acknowledge the technical assistance of H. R. Neal in certain phases of this investigation.

fering with the ability of the virus to establish itself. It is known that thyroxin secretion is greater upon exposure to cold and that the metabolic rate is thereby increased. Hence, a series of investigations was begun on three groups of five-week-old mice inoculated intracerebrally with 0.05 ml. of a 3-per cent suspension of infected brain-cord suspension and held at room temperature (22° C.). One group was given a daily dose of 0.5 mg. of thiouracil by mouth, a second group received 0.5 mg. of thyroid extract by the same method of administration, and the third group served as controls. The amounts of thiouracil, a recognized basal metabolism depressant, and thyroid extract fed to the animals were arbitrarily employed after a limited series of experiments to determine toxic doses. There was no visible indication that the amounts used were toxic.

During the course of this experiment C. W. Turner, of the University of Missouri, suggested and supplied a thyroactive iodocasein prepared by the method of Reineke and Turner (*3*) and referred to by Koger and Turner (*2*) as thyroprotein. A second set of three groups of five-week-old mice was infected with virus. One group was given 0.5 mg. of thiouracil and another group, 0.5 mg. of thyroprotein daily by mouth. The third group served as controls.

The results obtained to date have been quite encouraging. Infected five-week-old mice treated with thiouracil have invariably shown symptoms of paralysis and have succumbed earlier than the controls, whereas those given thyroid extract or thyroprotein have undergone incubation periods much longer than those of the controls (Table 1). The lengthy incubation periods attained with thyroprotein treatment imply that it is much more effective than thyroid extract. However, this may be due to failure at the present time to employ these two agents in doses containing identical amounts of thyroactive substance.

TABLE 1

THE EFFECT OF THIOURACIL AND THYROACTIVE SUBSTANCES ON SUSCEPTIBILITY OF SWISS WHITE MICE TO POLIOMYELITIS VIRUS

Number of mice in each group	Type of treatment after inoculation	Incubation time (days) required to effect 50 per cent mortality in each group
20	0.5 mg. thiouracil daily	5
8	0.5 mg. thyroid extract daily	11
36	0.5 mg. thyroprotein daily	14
20	Nontreated controls	7

Attempts to measure the effect of thiouracil, thyroid extract and thyroprotein on metabolism of the mice, employing techniques adapted to small animals, have not proved highly successful, but there is an indication that the thyroactive substances increase the metabolic rate considerably. Hence, an earlier suggestion (*1*) that the marked decrease in the incidence of poliomyelitis with the onset of cooler weather may be due in part to a change in the metabolism of the host seems to have gained support.

The effect of altered metabolism on resistance to poliomyelitis virus needs careful study. Normally, four- and five-week-old mice tend to be the most susceptible to the virus. Experiments in this laboratory have shown that thyroactive substances create longer incubation periods in mice of these ages than in older animals. Possibly there is a critical metabolism range for virus growth that can be exceeded quite readily by use of thyroid stimulants in four- and five-week-old mice, whereas older animals may have their lower normal metabolic rate elevated to the critical range upon thyroid stimulation and thus become more susceptible than they normally are. When more is known about tissue metabolism and the safety with which thyroactive substances can be administered, it is possible that these agents may have prophylactic value for certain age groups during epidemic periods of poliomyelitis.

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The Failure of Poliomyelitis Virus to Grow in Certain Protozoa of Sewage[1]

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C. Kling, who is well known for his studies of poliomyelitis in Sweden during the past 35 years, has estimated from tests made in 1939 that the amount of poliomyelitis virus in the sewage from a section of Stockholm having a population of 100,000 could reasonably be accounted for only if 100 per cent of the people were excretors of the virus or if the virus grew in sewage. He has rejected the former possibility (*1*) and has suggested that the virus probably grows in some microorganism of sewage, the most likely one being, in his opinion, protozoa of the genus Bodo.

Unaware of Kling's observations, we were also led to speculate on the possibility that poliomyelitis virus might grow in some microorganism of sewage, and during the past several years we have investigated this question.

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