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A Study of the Allergic Phenomena in the Central Nervous System.

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These experiments were designed to study the allergic response of the central nervous system and to determine what part this phenomena might play in certain types of meningitis and encephalitis. Tuberculous animals were first employed because it is known that their tissues are sensitive to tuberculin.

Guinea pigs were inoculated subcutaneously in the groin with a known quantity of virulent human tubercle bacilli sufficient to give rise to an extensive generalized tuberculosis within 3 to 6 weeks. At varying intervals, up to 5 weeks, following the initial inoculation different animals had injected in their subarachnoid spaces by the way of the basal cisterns 0.3 cc. of a 1/10, 1/100, and 1/1000 dilution of old tuberculin. If the animals failed to develop fatal central nervous system disturbances they were killed by means of decapitation under ether anesthesia. Gross and microscopic studies were made of the brain and viscera. Cultures were prepared of the brains for the presence of the tubercle bacilli and other pathogenic organisms. As controls, both tuberculous and non-tuberculous animals were employed in each experiment. In this investigation 112 guinea pigs were employed, 42 of which were controls.

Following the subarachnoid injection of tuberculin the animals with advanced visceral tuberculosis showed definite and constant clinical central nervous system manifestations as well as a striking histological response in the leptomeninges. Restlessness, ruffled hair, progressive weakness, twitching and loss of sphincter control occurred 3 to 4 hours after the inoculation of tuberculin. Death usually occurred within 6 to 12 hours. Histological studies of the brains revealed an extensive polymorphonuclear exudate in the subarachnoid space. In the more advanced cases there was a definite perivascular extension and some glial proliferation around the vessels of the cerebral parenchyma. The acuteness and severity of the meningitis was proportional to the duration and extent of the generalized visceral infection; the course paralleled the skin test.

Similar experiments were performed in which dead and living tubercle bacilli were substituted for tuberculin. The onset and development of the meningitis apparently differed only slightly from the animals inoculated with tuberculin.

Tuberculous guinea pigs inoculated with glycerin broth by the way of the basal cisterns showed no clinical manifestations, but in some there was found a slight meningeal exudate on microscopic examination. Similarly, the nontuberculous animals inoculated with tuberculin and glycerin broth showed no response either clinically or microscopically. All animals inoculated in the neck muscles and other parts of the body with tuberculin revealed no evidence of activity in the meninges.

These experiments demonstrate that the meninges of tuberculous animals react to tuberculin, as well as dead and living tubercle bacilli, by an exudative response suggesting an allergic phenomenon. Other experiments are in progress.

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Fate of the Active Agent in the Chicken Sarcoma in Mixtures Containing Inhibiting Substances.

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We have previously described[1] the presence of a tumor inhibiting substance in the filtrate of the Rous chicken sarcoma and in normal chicken sera. It was found that this inhibiting substance is retained in the supernatant fluid when the tumor filtrate is brought to pH 4, while the active agent is carried down in the precipitate. In a more recent report, Murphy[2] and his associates report results that would seem to confirm these observations.

The fact that the activity of the agent can be inhibited by the supernatant fluid and sera made it of interest to ascertain whether the agent was actually destroyed in such mixtures or whether its tumor producing properties were merely inactivated. In order to answer this question it became necessary to determine if it is possible to recover the agent in an active state from these non-infective mixtures. The supernatant fluid used was prepared by adding an equal amount of a phthalate buffer solution at pH 4 to a 20% filtrate

[1] Sittenfield, M. J., Johnson, B. A., Jobling, James W., PROC. SOC. EXP. BIOL. AND MED., 1931, **28**, 517.

[2] Murphy, James B., Helmer, O. M., Claude, Albert, Sturm, Ernest, *Science*, 1921, **73**, 266.