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Brain Reactions to Bacterial Filtrates Potent in Eliciting Local Tissue Reactivity.*

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The effects of bacterial toxins upon neuraxis have received the attention of many investigators. Studies of Claude¹ (tetanus toxin); Putnam, McKenna and Evans² (tetanus toxin); Lotmar³ (*Shigella dysenteriae*), and Branham and Lillie⁴ (experimental meningitis) are of direct interest.

In the work described below bacterial principles potent in the elicitation of the phenomenon of local tissue reactivity were used. All injections were given only intravenously, thus avoiding the possible mechanical injury to the brain. It was shown previously that, while in its usual form the phenomenon requires for elicitation the combined local preparatory and intravenous provocative injections, in some organs 2 intravenous injections 24 hours apart are capable of producing severe lesions (kidneys, intestines, etc.) (Apitz,⁵ Gerber,⁶ and Shwartzman.⁷) In the latter modification the first intravenous injection takes the place of the local preparatory injection of the former. The report deals with histological examinations of the brain of 11 rabbits. Each intravenous injection was given in a dose of 1 cc per kilo of body weight of bacterial filtrates variously diluted. One rabbit received one intravenous injection of meningococcus "agar washings" filtrate diluted 1:5 and died 24 hours later. In this animal there was found an acute meningococcus encephalitis. In addition to severe perivascular infiltration there were some independent foci beyond the vascular site in the tissues. They predominated in the cerebrum, were less conspicuous in the brain stem, were

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¹ Claude, H., *Arch. phys. norm. and pathol.*, Paris, 1897, **29**, 843.

² Putnam, T. J., McKenna, I. B., and Evans, J., *J. Psychol. and Neurol.*, 1932, **44**, 460.

³ Lotmar, F., *Nissl-Alzheimer Arb.*, 1918, **6**, 248.

⁴ Branham, S. E., and Lillie, R. D., *Pub. Health Rep.*, 1932, **47**, 1683.

⁵ Apitz, K., *J. Immunol.*, 1935, **29**, 255.

⁶ Gerber, I. E., *Arch. Pathol.*, 1936, **21**, 776.

⁷ Shwartzman, G., *Phenomenon of Local Tissue Reactivity and Its Immunological, Pathological and Clinical Significance*, Medical Book Department of Harper & Brothers, 1937, New York.

absent from the cerebellum and contained leuco-, lymphocytes and many tissue cells showing marked disintegration of the nuclei (Fig. 1). Myelin-stained sections of the frontal brain disclosed small foci of demyelination around the blood vessels (Fig. 2). The axons were swollen or destroyed. Another animal received 2 intravenous injections of meningococcus filtrate each in dilution 1:40 and died 24 hours after the second injection. There were foci of glia cells, histiocytes, leuco- and lymphocytes without any noticeable reaction around the blood vessels next to the ventricles but not in the fusion line. Two rabbits receiving single intravenous injections of meningococcus filtrate diluted 1:5 and 1:40 respectively, and 2 rabbits receiving each 2 injections of meningococcus filtrates diluted 1:5 and 1:40 respectively, showed an inflammatory irritation of the nervous system with pronounced changes in the glia cells and swelling of

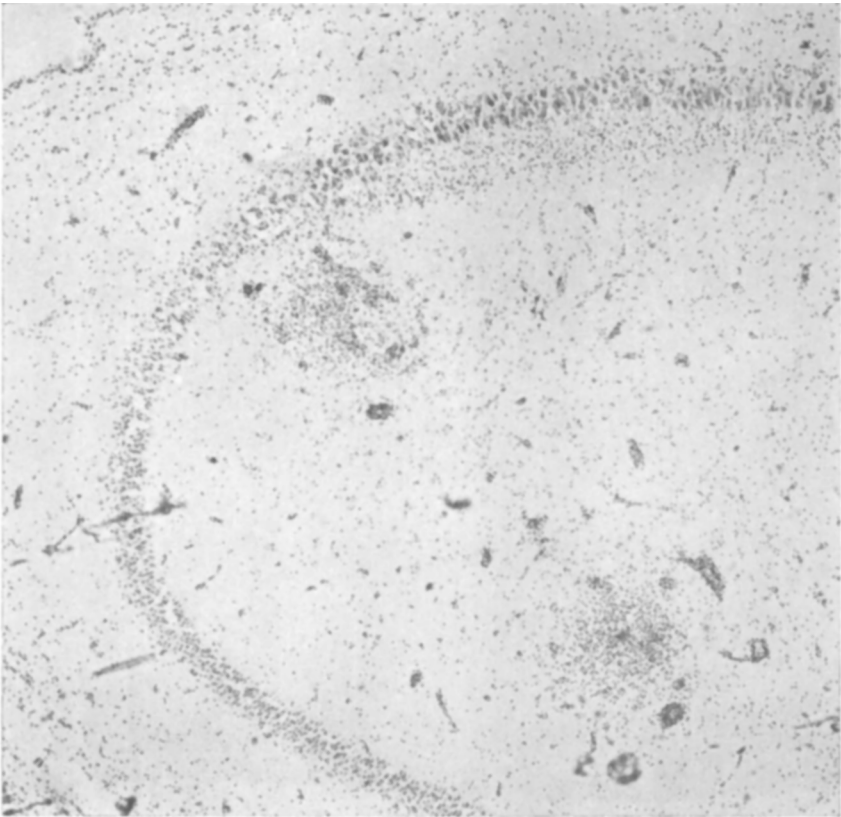


FIG. 1.
Rabbit 1: Foci in the hippocampal region. (Nissl stain.)

ganglion cells. Two rabbits receiving single intravenous injections of *Eberthella typhosus* "agar washings" showed only an increased number of damaged glia cells, mostly around the Purkinje cells and the molecular layer of the cerebellum. Two rabbits were injected with meningococcus toxin diluted 1:40 and reinjected 24 hours later with *Eberthella typhosus* toxin in dilution 1:10. They were killed 24 hours after the second injection. No lesions were found in the brain.

Thus, strong reactions scattered throughout the tissue itself of the entire brain and around the ventricles were similar to changes in the skin and kidneys of the phenomenon of local tissue reactivity. It is also noteworthy that the meningococcus toxin involved the white and gray matter alike.[†] Previous investigations showed that the phenomenon of local tissue reactivity deals with bacterial toxins capable of producing primary lesions in susceptible tissues. In tissues with natural resistance the preparatory effect of the first injection consists in the elicitation of reactivity permitting the production

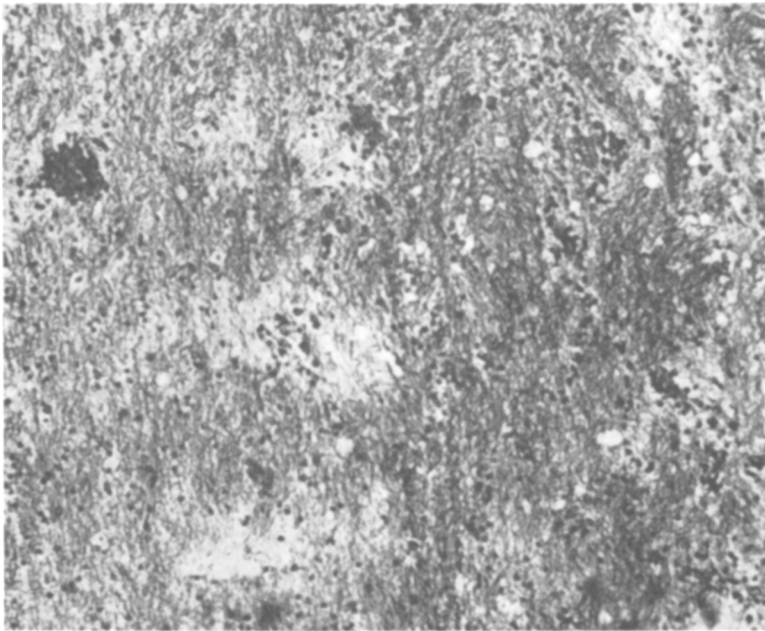


FIG. 2.
Rabbit 1: Frontal brain, demyelination. (Heidenhain stain.)

[†] According to Lotmar³ (Fig. 3) *Shigella dysenteriae* toxin damages the gray matter. The tetanus toxin, according to Claude¹ and to Putnam, McKenna and Evans,² affects rather the white matter.



FIG. 3.
Rabbit 2: Foci around the ventricle. (Haemalum and eosin stain.)

in the prepared sites of severe lesions by means of the following provocative injections. In this manner "normal" endogenous bacterial inhabitants may evoke serious damage in refractory tissues and organs. A single intravenous injection and invasion of the blood stream by bacteria may induce damage in tissues and organs made previously reactive by the presence of spontaneous infections.⁷

The only conclusion now possible is that the bacterial filtrates potent in the elicitation of the phenomenon of local tissue reactivity may also produce severe damage in the brain of rabbits by way of the blood stream. The possible enhancement and modification of the character of lesions seen in the phenomenon in other organs have not been ascertained as yet in studies on the brain.