

stance. It is an interesting observation in comparative cellular requirements that methionine does not replace cystine in the stimulation of gonococcus growth. This cystine requirement of the gonococcus was found to be only a type requirement; certain other substances containing sulfur, and potentially -SH formers, satisfactorily replaced this amino acid. Among these were cysteine hydrochloride, glutathione, thioglycolic acid, flowers of sulfur and barium sulfide.

Summary. A rapid and heavy growth of meningococcus developed on an agar medium containing tryptic digest of casein, dextrose and buffer at pH 7.4-7.6. However, this medium failed to support growth of the gonococcus. Addition to the medium of a small amount of cystine, however, stimulated growth of this organism. The growth of gonococcus on this casein digest medium, with cystine, was as heavy as that of meningococcus. The growth of meningococcus did not seem to be improved by this addition of cystine to the medium.

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Susceptibility to Convulsions in Relation to Age. II. Influence of Bile in Rats.

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In a previous communication a hypothesis was developed that the high susceptibility to convulsions of infants and young children may be due to the action of irritants entering the brain in the absence of a hypothetical hematoencephalic barrier.¹ Thus, it was observed that acid fuchsin, a water soluble neurophilic, sulfonated dye, will produce convulsions in rats of from 17 to 20 days of age and not thereafter. This phenomenon may be associated with the ability of acid fuchsin to penetrate the brain of the young animals and not of adults.

In the attempt to obtain further information concerning this peculiarity of the young brain, the influence of bile was studied. It has been known for some time that the brains of young children dying with jaundice may be icteric, while those of severely jaundiced adults are not.² Also, it has been observed that jaundiced infants

¹ Frohlich, A., and Mirsky, I. A., *Arch. Neur. and Psych.*, 1942, **47**, 30.

² Orth, J., *Virch. Arch. f. Pathol. Anatomie*, 1875, **63**, 447.

TABLE I.
Susceptibility to Convulsions in Different Age Groups after Administration of Bile.*

Age	No.	Dose mg/g	No. with convulsions	% dead
1-5	37	0.1-0.5	34	12
6-10	16	0.1-0.5	13	6
11-15	11	0.3-1.0	0	0
16-adult	22	0.5-1.0	0	0

*Parke Davis & Co. "Concentrated Bile."

may develop convulsions.³ These factors seemed to warrant an attempt at experimental elucidation.

Experimental. Groups of rats of both sexes which ranged in age from 1 day to over 100 days were tested with various doses of bile (prepared from Parke Davis & Co. "Concentrated Bile"). Table I indicates the number of animals employed in each age group. The bile was administered intraperitoneally in a 1% solution, and the dosage varied from 0.1 to 1 mg of bile per gram of body weight. No irritation was apparent as a consequence of the injection of bile.

The incidence of convulsions is detailed in Table I and illustrated in Fig. 1. Within 100 minutes after the intraperitoneal injection of bile, convulsions occurred in 92% of rats between the ages of 1 and 5 days, and in 81% of rats between the ages of 6 and 10 days. These convulsions would last several hours and in a few instances terminated with the death of the animal. The convulsions were gradual in onset. The early abnormal signs were an increase of reflex activity, and much "wriggling" of the animal. This was followed by rhythmic clonic seizures during which the animal shrieked. Tonic contractions of the abdominal wall occurred frequently. Consequent to the full development of the convulsions the animals became somewhat lethargic and would remain in one position for several hours. They were then returned to their mothers and when examined 18 hours later no abnormality could be observed.

The intraperitoneal administration of bile to animals older than 10 days of age caused no apparent disturbance. However, when 1 mg of bile in a 1% solution was introduced directly into the brain by way of a trephine opening, clonic convulsions began within 10 minutes. Histological examination of the brains of bile-treated animals up to 10 days of age occasionally revealed the presence of pigment in various parts of the brain within two hours of the injection. The pigment was observed in greatest concentration in the

³ Zimmerman, H. M., and Yannet, H., *Am. J. Dis. Child.*, 1933, **45**, 745.

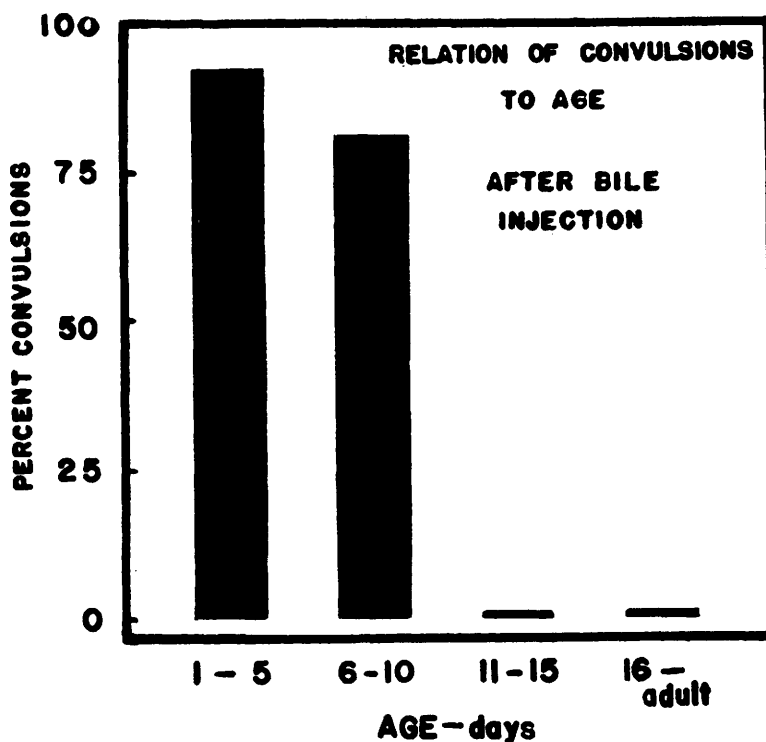


FIG. 1.

Illustrating the relation of age to the development of convulsions consequent to the injection of bile.

periventricular areas of the cornu ammonis.* Examination of the brains of the adult animals after the intraperitoneal injection of bile revealed no pigment.

The syndrome of "Kernicterus" has been known for some time² but has received relatively little attention. In the majority of such cases reported in the literature biliary pigment was found in the interstitial tissue of the cornu ammonis, in the cerebral cortex and in the cells of the basal ganglia. Zimmerman and Yannet³ reported that convulsions or spasticity occurred in more than 40% of such cases. Other evidences of cerebral involvement were observed in many of the other cases.

Our studies with rats support the hypothesis that a hematoencephalic barrier is present in older animals and not in the very young. The reason for the cessation of response to bile in rats at 10 days of age and to acid fuchsin at 17 to 20 days of age is not clear.

* We are indebted to Dr. I. Mark Sheinker of the Laboratory of Neuropathology, University of Cincinnati College of Medicine, for performing the histological studies.

These considerations suggest that the increased susceptibility of infants to convulsions is associated with the ease with which various irritants can enter the brain tissue. However, another factor also must be considered. It is probable that not only is it much easier for various substances to enter the central nervous system of the young, but that this organ is much more sensitive to irritants. Thus, Brill and Seidemann⁴ have observed that the electroencephalograms of normal children show a considerable tendency to dysrhythmia during hyperventilation and that this tendency diminishes with advancing age. It is probable that in the presence of increased tissue susceptibility, as indicated by cerebral dysrhythmia, and in the absence of a hematoencephalic barrier, as indicated by the passage of bile and dyes into the brain, a toxic agent will produce seizures in young subjects when it would be ineffective in older ones.

Summary. The intraperitoneal injection of bile results in the production of convulsive seizures in rats up to 10 days of age and not thereafter. The intracerebral injection of bile produces convulsions in adult rats. The hypothesis is developed that young animals are more susceptible to convulsive seizures because of an inherent cerebral dysrhythmia and a deficient hematoencephalic barrier.

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Subarachnoid Injection of Thiamine in Cats; Unmasking of Brain Lesions by Induced Thiamine Deficiency.

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This work was undertaken to determine whether the neurological symptoms of thiamine deficiency could be treated more effectively by introduction of the vitamin into the subarachnoid space than by the usual routes of administration. It seemed possible that thiamine might be held up or delayed at the hemato-encephalic barrier when given by the usual routes. Stern¹ has made a rather exuberant report of the effectiveness of subarachnoid injection of thiamine in patients with a variety of diseases.

⁴ Brill, N. Q., and Seidemann, H., *Am. J. Psych.*, 1941, **98**, 250.

¹ Stern, E. L., *Am. J. Surg.*, 1938, **39**, 495.