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Isolation of a Virus from an Acute Encephalitis Case in Peiping.

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While the recent occurrence of acute encephalitis in North China has attracted some attention of the clinicians,[1] the etiological agent has hitherto not been isolated. In view of the epidemiological interest it seems of importance to determine whether the etiology of acute encephalitis encountered locally is a known virus such as the Japanese type B and the St. Louis type, or a new type of virus. In the present communication observation made on a virus isolated from a case of acute encephalitis is briefly described.

The patient, a Chinese boy, 9 years of age with a 2-day history of fever, repeated vomitings and attacks of convulsions, was admitted to the Peiping Union Medical College Hospital on September 23, 1940. Blood and spinal fluid cultures made at this time failed to show growth of organisms. The spinal fluid was slightly cloudy and contained in one cu mm, 46 white blood cells which are chiefly lymphocytes. The patient died on the 4th day of fever. On post-mortem examination essentially normal findings except for the gross appearance of congestion of the vessels of the central nervous system were seen. Sections of the brain showed presence of widely scattered areas of perivascular infiltration with lymphocytes. A portion of the brain was ground with sterile sand and made up to 10% suspension with sterile meat infusion broth (pH 7.6). The suspension was then centrifuged at 3,000 r.p.m. for 15 minutes. 0.025 cc of the supernatant was inoculated intracerebrally and separately to 7 Swiss mice, each weighing about 15-17 g. Beginning from the 5th day after inoculation, 2 of the animals began to show tremor, spasm and weakness of the limbs which became paralyzed on the 6th day and finally died on the 7th day; the remaining 5 became sick with roughened hair and hunched body without showing tremor or paralysis and died between 5th and 7th days. Paraffin sections of brains from animals dying from the infection showed numerous areas of perivascular lymphocytic infiltration. The choroid plexuses, meninges and the visceral organs appeared normal.

[1] Kuttner, A. G., and T'ung, T., *J. Clin. Invest.*, 1936, **15**, 525; Chu, F. T., Wu, J. P., and Teng, C. H., *Chinese Med. J.*, 1940, **58**, 68; Huang, C. H., and Liu, S. H., *Chinese Med. J.*, 1940, **58**, 427.

Brain from the infected mice dying from 5-7 days was found to be infective for normal Swiss mice, as little as 0.025 cc of a 1:100,000 dilution of a brain injected intracerebrally being sufficient to cause death of these animals in 5-7 days, usually accompanied with symptoms of tremor or paralysis. By intracerebral inoculations the infection has been passed from mouse to mouse for more than 12 generations. In all instances the infection regularly occurred and the same pathological findings as those found in the primary mouse passage were present. On several occasions the infected brain suspensions were first filtered through "V", "N" and "W" Berkefeld filters or Seitz E.K. pads before intracerebral inoculations were made. The filtrate produced the same kind of picture of infection in Swiss mice as those caused by the unfiltered suspensions. The infective agent has remained potent when kept in 50% glycerin for 2 months although a drop of the infective titer was seen after 3 weeks of preservation. In ordinary broth suspensions, however, the infectivity rapidly deteriorated in a few days. It seems clear that the infective agent recovered from the brain of the encephalitis patients behaved like one of the filterable viruses, and is therefore designated as Peiping Encephalitis Virus No. 1 (P. E. No. 1).

Rabbits, guinea pigs, white rats and Chinese hamsters were found to be resistant to the P. E. virus either by intracerebral or intraabdominal inoculations with the infected mouse brain. However, no attempt was made to establish the infection by repeated animal to animal passage in these species.

A monkey *(Macacus rhesus)* was found to be susceptible to intracerebral inoculation with this virus; the animal developed fever and tremor after an incubation of 6 days and finally died on the 10th day.

By repeated intraäbdominal inoculations with the infected mouse brains, rabbits failed to succumb to the infection but developed potent antiviral antibodies in their sera. By similar procedures, neutralizing sera against Japanese type B. S.K. (Hashimoto)* and St. Louis No. 3 (Webster)* encephalitis viruses were separately prepared from rabbits for testing with the Peiping encephalitis virus. It was found that the Japanese S.K. virus antiserum neutralized the homologous and the Peiping viruses in about equal titer, while the St. Louis virus antiserum was able to neutralize only its homologous virus but not the Peiping virus. On the other hand, the Peiping

* These viruses originally obtained from Dr. Hashimoto and Dr. Webster, were kindly supplied to us by Dr. J. P. Wu, Division of Pediatrics, Peiping Union Medical College.

virus antiserum was able to neutralize not only the homologus virus but also over 100 MLD of the Japanese B virus and partially 10 MLD of the St. Louis virus.

Conclusion. A virus (Peiping encephalitis virus) capable of producing encephalitis in Swiss mice and a monkey was isolated from a case of acute encephalitis. On the basis of animal pathogenicity and virus neutralization tests, the virus is considered to behave like the Japanese type B virus, but to be serologically distinguishable from the St. Louis encephalitis virus.

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Comparative Anticonvulsant Activity of 1-Diethylacetyl-5, 5-Cyclopentamethylene Biuret, Sodium Diphenyl Hydantoinate and Sodium Pentobarbital in Mice.*

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The structural features which appear to account for the hypnotic action of the barbiturates are the presence of a –CONH– group[1] and an alkyl or acyl group replacing both hydrogen atoms in position 5.[2] Recently Hill and Degnan[1] have emphasized that the alkyl biurets have 2 –CONH– groups within their structure. They postulated that an acyl biuret containing branched chain alkyl groups might have hypnotic properties and low toxicity. Although Hesse and Taubmann[3] had previously reported on the pharmacology of certain biurets and some of their guanyl and thio derivatives, the use of these agents as hypnotics had not been proposed. They reported that guanyl-thiourea lowered the body temperature of rabbits in which artificial fever had been produced. The antipyretic action was believed to be due to increased heat loss and was abolished when animals were kept in a warm environment. The presence of the thio group seemed necessary for antipyretic action. When oxygen or an amino group was substituted for the thio group antipyretic action

* Sodium pentobarbital was supplied through the courtesy of Eli Lilly and Company, Indianapolis, Indiana.

1 Hill, A. J., and Degnan, W. M., *J. Am. Chem. Soc.*, 1940, **62**, 1595.

2 Tatum, A. L., *Physiol. Rev.*, 1939, **19**, 472.

3 Hesse, E., and Taubmann, G., *Arch. f. Exp. Path. u. Pharmakol.*, 1929, **146**, 113.