ARTICLE 8—MEETINGS

The Association shall hold an annual meeting at such time and place as may be determined by the Council. Other meetings of the Association and of the Sections may be authorized by the Council. The Divisions and the Branches may hold annual and other meetings.

ARTICLE 9—PROCEEDINGS

The proceedings of the Association and the list of officers and members shall be published in such manner as the Council may direct.

ARTICLE 10—FUNDS

The Permanent Secretary shall collect the annual dues and make expenditures as directed by the Council. The Treasurer shall deposit or invest the permanent funds of the Association, as provided for trust funds by the laws of the state of Massachusetts or the state of New York. Bequests and gifts will be administered in accordance with the provisions of the donors. The payments from sustaining and life members form part of the permanent fund, and the income (after the death of the member) shall be used for research, unless otherwise directed by unanimous vote of the Council or by a majority vote at two consecutive annual meetings.

ARTICLE 11—ALTERATION OF THE CONSTITUTION

This Constitution may be amended at a general session by unanimous vote or by a majority vote at two consecutive annual meetings.

SPECIAL ARTICLES

FETAL ENCEPHALOMYELITIS: PRENATAL INCEPTION OF INFANTILE TOXOPLASMOSIS[1]

HUMAN toxoplasmosis, first encountered as an encephalomyelitis in infants and verified by the experimental transmission of the infection to animals (Wolf, Cowen and Paige, 1939),[2, 3, 4] has since been found to produce an encephalitis in older children (Sabin, 1941),[5] and a predominantly pulmonary infection in adults (Pinkerton and Henderson, 1941),[6] the organism again having been successfully isolated in each instance. Although toxoplasmosis is known to be widespread among rodents and birds, the manner in which man acquires the infection has not yet been discovered. From the first, however, it had been felt that the infantile form of the disease was congenital.[3, 7, 8, 9, 10] The symptoms and signs began at birth or shortly thereafter. The chronic appearance of the pathological lesions, which were often extensively calcified, made it unlikely that they could have developed during the short extrauterine period. These findings suggested that the disease had begun as a fetal encephalomyelitis.[3, 7]

The considerations which weighed against this assumption were: (1) the mothers were all apparently healthy and some had had healthy children prior and subsequent to the birth of the infected child, (2) evidence of placental infection was lacking, and (3) evidence of the occurrence of adult human toxoplasmosis had not been furnished. The last objection is now overcome with the recent demonstration of adult toxoplasmosis.[6, 11] The first inconsistency, the fact that the mothers seemed healthy, may mean, as has been suggested elsewhere, that they harbored a latent infection. The common occurrence in lower animals of such clinically inapparent toxoplasmic infestation would lend support to such a possibility. Placentas have not, as yet, been available in these human cases, except in one instance in which the poor state of preservation made it unsatisfactory for study.

The suspicion that this infantile encephalomyelitis begins before birth is not original with the authors. Three cases[9, 10, 12] identified from the literature and reclassified as infantile toxoplasmic encephalomyelitis[3, 7, 8] were considered by the original authors to be instances of congenital disease, although proof was lacking.

Information acquired from additional cases coming to autopsy in this institution and further experimental data, which will be reported in detail elsewhere,[13] prove that infantile toxoplasmosis may begin as a fetal encephalomyelitis. One infant (B.R.) had given evidence of hydrocephalus *in utero*, necessitating cranioclasia for delivery. The child was born at term, was normally developed, except for the enlarged head, and was viable up to the time of delivery. The stillborn child on pathological examination presented an advanced toxoplasmic encephalomyelitis with extensive calcification of the lesions and an associated chorio-

[1] Supported in part by grants from Child Neurology Research (Friedsam Foundation) and the Matheson Commission.

[2] A. Wolf, D. Cowen and B. H. Paige, SCIENCE, 89: 226, 1939.

[3] *Idem, Am. Jour. Path.*, 15: 657, 1939.

[4] *Idem, Jour. Exp. Med.*, 71: 187, 1940.

[5] A. B. Sabin, *Jour. Am. Med. Assoc.*, 116: 301, 1941.

[6] H. Pinkerton and R. G. Henderson, *Jour. Am. Med. Assoc.*, 116: 807, 1941.

[7] A. Wolf and D. Cowen, *Bull. Neurol. Inst. N. Y.*, 6: 306, 1937.

[8] *Idem, Bull. Neurol. Inst. N. Y.*, 7: 266, 1938.

[9] J. Jankû, *Casopis lekarew ceskyck*, 62: 1021, 1923.

[10] C. M. Torres, *Compt. rend. Soc. Biol.*, 97: 1778, 1787, 1797, 1927.

[11] H. Pinkerton and D. Weinman, *Arch. Path.*, 30: 374, 1940.

[12] R. Richter, *Arch. Neurol. and Psychiat.*, 36: 1085, 1936.

[13] B. H. Paige, D. Cowen and A. Wolf. In preparation.

retinitis. Toxoplasmata were abundant in the lesions. In this instance, there can be no doubt that the infection was acquired during intrauterine life. Another infant (L.M.) came to autopsy recently with the typical lesions of toxoplasmic encephalomyelitis, which was verified by transmission of the infection to animals from postmortem material. An obstructive hydrocephalus, obviously due to the infection, noted two hours postpartum, points to the prenatal inception of the disease.

In an attempt to ascertain the existence of maternal infection, tests for neutralizing antibodies[14] in the blood of the mothers have been begun. The mothers of the above two infants with proven toxoplasmosis have been studied. Their sera, normal control sera and physiological saline solution were mixed with varying dilutions of mouse brain suspension infected with Toxoplasma, and inoculated intradermally into rabbits. The development of typical Toxoplasma skin lesions was used as an indicator. There was definite inhibition of the formation of such lesions by the sera of the mothers of the infected children. This demonstration of maternal neutralizing antibodies lends further support to the probability that infantile toxoplasmosis is of prenatal orrigin.

This disease of the central nervous system in infants has a specific pathological picture characterized by necrotizing chronic inflammatory lesions, miliary granulomata, conspicuous calcification, frequent hydrocephalus and focal chorioretinitis.[3, 7, 8] The absence of major developmental anomalies of the brain indicates that the infection, when congenital, probably begins late in fetal life.

The symptoms and signs of widespread cerebral damage, roentgenographic evidence of internal hydrocephalus and cerebral calcification, the ophthalmoscopic observation of a striking chorioretinitis, and the presence in the blood of neutralizing antibodies to Toxoplasma, have led to the clinical diagnosis of several new cases also to be reported later. Of these children, two (P.D. and A.I.) have survived to the ages of 4 and 2 years, each giving anamnestic evidence of the disease early in infancy. These children are mentally deficient, and one, subject to convulsions, had been regarded as an epileptic. It is quite probable that such instances of infantile toxoplasmic encephalomyelitis, which survive with severe cerebral damage, may be erroneously classified as congenital malformation of the brain, birth injury, epilepsy, congenital hydrocephalus, etc. It is desirable to separate instances of this specific, congenital infection from these heterogeneous groups, since the hope of successful therapy depends upon their recognition. It would seem especially important to detect the inapparent infection of the mother in order to prevent the disease in the child. It is hoped that serological tests and eventually a curative agent will make this possible.

[14] A. B. Sabin and P. K. Olitsky, SCIENCE, 85: 336, 1937.

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EXPERIMENTAL ANTI-PERNICIOUS ANEMIA FACTOR DEFICIENCY IN DOGS

IN the course of studies on intestinal absorption in dogs with "internal" bile fistulae (anastomosis of the gall bladder to the right renal pelvis with ligation of the common bile duct) we have observed the spontaneous development of an anemia. Further careful study has shown the anemia to be of the macrocytic hyperchromic type.

Normal values for red count, hemoglobin, mean corpuscular volume (MCV), mean corpuscular diameter (MCD) and mean corpuscular hemoglobin (MCHb), have been established, as shown in Table 1. The values for dogs kept 6 months or more on our stock diet do not differ significantly from those of animals newly received.

TABLE 1

ERYTHROCYTE CHARACTERISTICS IN NORMAL DOGS

	Number of observations	Number of dogs	Mean	Standard deviation
Red cell count (millions/mm³)	49	25	6.2	0.7
Hemoglobin (grams per 100 ml.)	49	25	12.9	1.8
Mean corpuscular volume (cubic micra)	49	25	71.3	4.4
Mean corpuscular diameter (micra)	19	18	6.7	0.1
Mean corpuscular hemoglobin (micro-micrograms)	49	25	20.9	1.6

Having established the normal blood picture of dogs in this laboratory it also became necessary to set up criteria for an experimentally produced anemia resembling the human macrocytic hyperchromic anemias, such as pernicious anemia and sprue. It is now generally accepted that this type of anemia in man is due to lack of a factor present in liver, which has been termed the anti-pernicious anemia (APA) factor or erythrocyte maturation factor. Such a deficiency is believed to be produced in man either by failure of intestinal absorption (sprue), lack of intrinsic factor in the gastrointestinal tract (pernicious anemia) or by disease of the liver and consequent inability of that organ to store the APA factor produced by reaction between intrinsic and extrinsic factors (macrocytic anemia of human liver disease). No matter in which way the normal chain of events is interrupted, the result is an increase of MCV, MCD and MCHb above