TABLE I.

	No. animals	Duration of experiments hr	Adrenal: Cholesterol, g %	Adrenal: Ascorbic acid, mg %
Normal.				
Controls	23	—	4.03 ± 0.10	370 ± 14
Epinephrine. 1 × 0.02 mg/100 g subcut.	6	2.0	2.88 ± 0.28	210 ± 24
Epinephrine. 4 × 0.02 mg/100 g subcut.	10	4.0	2.26 ± 0.22	216 ± 9
Epinephrine. 0.02 mg/100 g/hr intraven.	6	2.0	2.31 ± 0.18	104 ± 17
Hypophysectomized.				
Controls	4	—	5.74 ± 0.43	398 ± 38
Epinephrine. 4 × 0.02 mg/100 g subcut.	9	4.0	5.34 ± 0.47	411 ± 13
Epinephrine. 0.02 mg/100 g/hr intraven.	2	2.0	6.04	357

At the moment it is not possible to decide whether this effect of epinephrine is due to a direct stimulation of the cells of the anterior pituitary that secrete adrenotrophic hormone or whether it is due to changes in the composition of the blood acting as the exciting agent. Further experiments to clarify this question are in progress.

14985

The Incidence of Toxoplasmic Infections in the St. Louis Area.*

WILLIAM P. CALLAHAN, JR. (Introduced by Robert A. Moore.)

From the Department of Pathology, Washington University School of Medicine, St. Louis, Mo.

Since 1940 8 fatal cases of toxoplasmosis have been observed in the St. Louis area.[1,2,3] Two of the patients were adults, in whom the infection occurred as an acute febrile disease manifested by a skin rash and closely simulating the typhus spotted fever group of diseases. A history of tick bite was obtained from both patients.[1] The other instances of this type of infection have been observed in infants in whom the onset of clinical signs and symptoms was apparent at birth or appeared shortly thereafter.[2,3] Widespread involvement of the central nervous system gave rise to the principal clinical manifestations of generalized convulsions, muscular paralysis and internal hydrocephalus. Cerebral calcification and widespread encephalomyelitis with the formation of many granulomatous lesions were the prominent pathologic changes. Toxoplasma were present in small aggregates or pseudocysts and as free organisms within the central nervous system.

The onset of the disease at birth or shortly thereafter, as well as the advanced nature of the lesions in the central nervous system, led Paige, Cowen, and Wolf[4] to advance the concept of the intrauterine inception of the disease. In the cases reported by these observers, as well as many other instances of the infantile type of toxoplasmic encephalomyelitis, the infection in the mother produced no clinical manifestations of disease although neutralizing antibodies were demonstrated in the peripheral blood.[5,6,7] This would indicate

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that inapparent or subclinical infections may be present and unrecognized unless pregnancy occurs and the infection is transferred to the fetus where it produces irreparable damage.

Since a relatively large number of instances of the infantile type of toxoplasmic infection have been observed in the St. Louis area it may be postulated that inapparent infections in adults may be common. In an attempt to determine the incidence of toxoplasmic infections in this vicinity, neutralization tests were performed on the blood serum of 100 apparently normal individuals between the ages of 18 and 28 years. Because of the possible intrauterine inception of the disease it was thought that a survey including individuals in the child-bearing age from St. Louis should be made, using as a control group persons of the same age from a different locality. Blood was obtained from 26 unmarried girls between the ages of 17 and 24 years who lived outside of the state of Missouri; from an equal number of unmarried girls in the same age group who had been residents of St. Louis since birth; and from 25 married women in the same age group who had one or more normal children. Blood was also obtained from 23 men between the ages of 20 and 28 years.

Blood. Blood was drawn from the antecubital vein under sterile conditions. In most instances, because of the difficulty in obtaining out-of-state residents, a large number of blood samples were drawn at the same time. The blood was placed in sterile Kolmer tubes and allowed to clot at room temperature for 20 minutes. It was then centrifuged for 10 minutes and the serum withdrawn by means of a sterile pipette and placed in soft glass vials. These vials were sealed, labeled and rapidly frozen. They were stored in an insulated box containing solid carbon dioxide. The serum obtained from each individual was then placed in at least 2 vials to allow repetition of the test whenever necessary. Whenever possible, serum was used the day it was obtained and was stored in a refrigerator at 4°C. Under no circumstances was the serum allowed to stand in a refrigerator, without freezing, for more than 24 hours.

Animals. Well nourished, healthy rabbits weighing 3-5 kg were used. Animals with clear skin were selected and preferably white New Zealands were used because of the uniform color of the skin and the ease with which the subsequent reactions could be read. No naturally immune rabbits were encountered. All animals, with the exception of 2, were obtained from one dealer. The backs of the animals were clipped with OO Oster clippers and then carefully shaved with a straight razor. The shaved area was then carefully marked with India ink into 20 squares.

Organism. Through the courtesy of Dr. Abner Wolf the B.D. strain of Toxoplasma, isolated from a fatal human case, was obtained. The organism was maintained by intracerebral inoculation of mice with a 10% suspension of infected mouse brain in veal infusion broth. The organism was passed serially for one month, before it was used for neutralization tests, to determine the relative pathogenicity of this strain. It was found that intracerebral inoculation of .04 cc of a 10% mouse brain suspension produced convulsive seizures on the fourth day and was uniformly fatal on the fifth day. The brains of the mice succumbing on the fifth day after intracerebral inoculation were cultured and found to be bacteriologically sterile. Touch preparations stained by the Wright and Giemsa methods were examined to make certain of the presence of large numbers of Toxoplasma.

Neutralization Test. The method used is similar to that described by Sabin[6] except for several minor alterations. Two whole mouse brains, removed under sterile precautions from infected animals on the fifth day, were ground in a mortar without an abrasive and enough veal infusion broth was added to make a 10% suspension. This was allowed to sediment spontaneously for 15 to 20 minutes in a refrigerator at approximately 6°C. Cultures were made on rabbit's blood agar to determine the presence of any contaminating bacteria. The supernatant fluid was regarded as a 1:10 dilution. From this 1:50, 1:100, 1:500, and 1:2500 dilutions were made using veal infusion broth as the diluent. An equal amount of the undiluted serum to be tested was added to each dilution of the organism making mixtures of 1:20, 1:100, 1:200, 1:1000 and 1:5000. After thorough mixing they were

allowed to stand at room temperature for 30 minutes. Two hundredths cubic centimeters of each mixture was then injected intracutaneously into the skin of the rabbit within the previously marked squares.

Interpretation of Neutralization Test. Human sera produced erythema in the rabbit's skin within 24 hours, but the zone of redness disappeared by the third or fourth day. The lesions produced by Toxoplasma appeared by the end of the fifth day and consisted of maculopapular eruptions surrounded by a zone of erythema. By the eighth day the lesions resulting from the larger concentrations of organisms underwent central necrosis and the results were determined on the ninth day. Each lesion was accurately measured, drawn on transparent paper and described. Careful records were kept of the time of disappearance of the erythema, the appearance of the toxoplasmic lesions and the interval to the production of necrosis, to evaluate any individual variations in the type of reaction on different rabbits. By the fourteenth day the lesions produced by the more dilute mixtures began to blanch and the necrotic lesions became encrusted. The animals usually died by the twenty-first day. Any reactions which could not be interpreted as conclusive were repeated on other animals.

Results. The serum of 2 individuals prevented the production of necrotic lesions in the skin of rabbits. These 2 persons were residents of the St. Louis area and had lived in this vicinity all their lives. Careful physical examinations were performed and were entirely negative. Examination of the eye grounds showed no pathologic lesions. A complete medical history was taken and no history of present or past illness was obtained that might be interpreted as a toxoplasmic infection. Both individuals were unmarried girls of 18 and 21 years respectively. No positive tests were obtained from the group of unmarried non-residents, the married women, or from any of the men tested in this series.

Conclusions. The sera of 2.7% of the individuals in the St. Louis area that were tested showed the presence of a definite inhibitory factor on the necrotizing action of Toxoplasma in the skin of rabbits.

14986 P

Human Thyrotoxicosis: Response to Para-Aminobenzoic Acid.

LOUIS BERMAN. (Introduced by S. Ansbacher.)

Office and Laboratory at 1050 Park Avenue, New York City.

The use of thiourea and especially of thiouracil in the treatment of hyperthyroidism was first suggested by Astwood.[1] Apparently, these compounds prevent thyroid hormone synthesis and numerous papers[2] have appeared showing that they are effective in mild or moderately severe cases of thyrotoxicosis and in the preoperative preparation of patients for thyroidectomy.[3] The disagreeable taste of thiourea makes thiouracil the preferred therapeutic agent, although the latter has been demonstrated clinically to give untoward reactions, including agranulocytosis,[1] myxedema,[4] skin eruptions, fever, and jaundice.[5,6] Indeed, according to a most recent report,[7] "Thiouracil is an effective drug for the treatment of thyrotoxicosis. It is also an unpredictable toxic drug which may produce serious and uncontrollable effects, especially on the bone marrow and liver."

In view of the ever increasing clinical appli-

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