THE OCULAR MANIFESTATIONS OF CONGENITAL TOXOPLASMOSIS IN FIVE OUT OF 686 CASES OF MENTAL DEFICIENCY EXAMINED IN A STATE INSTITUTION FOR MENTALLY RETARDED CHILDREN, KINSTON, NORTH CAROLINA, U.S.A.

By

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TOXOPLASMOSIS is an infectious disease caused by a protozoal parasite of world-wide geographic distribution. The organism, *Toxoplasma gondii*, has been known since 1908, when it was demonstrated in the gondi, a North African rodent, by Nicolle and Manceaux and independently by Splendore in the rabbit in Brazil. Benda quotes Hellbrügge as mentioning that Toxoplasma apparently had been discovered in 1900 by Laveran, in the blood of a bird. It has since been found to be an infective agent in a great variety of species of rodents, mammals and birds from almost any part of the world, providing a large reservoir for human infection.

The rat, mouse, dog, hen, cow, goat, pig, sheep and many more display host susceptibility to the toxoplasma parasites, and serological evidence indicates that it has been responsible for infecting between 20 per cent. and 40 per cent. of the population in Britain (Beattie). The incidence of congenital toxoplasmosis in State Schools for Mental Defectives in the U.S.A. has been estimated at ranging from 0·2 per cent. to 0·05 per cent.

The first cases of proven human infection were detected in new-born infants by Wolf and Cowen in 1937. The parasite is crescentic-shaped, usually found in cells where it reproduces by fission. It shows a pronounced preference for chorio-retinal structures of the eye where it was observed by Wilder, Jacobs and others. Hogan was able to isolate the parasite from the eye of a case of congenital toxoplasmosis of twenty years' duration.

Aggregates of toxoplasma, often referred to as cysts, have been noted in sections of the brain, spinal cord, pancreas, lungs, liver, kidneys, supra-renals, gonads, myocardium and skeletal muscles. There the parasites may remain viable in the encysted stage for a long time, if not for the life of the host. The parasites are not infrequently released from the cyst walls, inducing a parasitaemia or localized inflammatory changes and scars in the uveal structures. This has been suggested to be the mechanism whereby recurrent attacks of human toxoplasmic chorio-retinitis are produced.

By means of the cytoplasm-modifying methylene-blue dye test developed

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by Sabin-Feldman, complement-fixation test and toxoplasmin skin test, it has been demonstrated that patients with uveitis yield a higher proportion with immunological evidence of toxoplasmosis than is detectable in the general population. The fact that positive findings are recorded in the normal population, shows the widespread nature of this disease.

Toxoplasmosis, on the whole, does little harm in the adult population except in the acquired form which may be fatal. The human foetus, however, is particularly susceptible to the parasites which display a remarkable affinity for the central nervous system. The disease is transmitted at about the 5th month of pregnancy to the foetus through the placental circulation from a mother who has suffered from a recent infection. The disease, however, is usually subclinical and mild and rarely recognized. Such a mother may give birth to a child with signs of hydrocephaly, mental deficiency, microcephaly, epilepsy, chorio-retinitis, microphthalmia, optic atrophy and muscle paralysis. The mother usually develops immunity to the organism and rarely, if ever, has two children with the same disease. The new-born infant may show additional evidence of active infection by such signs as hepatomegaly, splenomegaly, icterus and a maculo-papular rash.

There has been much discussion about the level at which dye titres become of clinical significance. One sees, for example, children with convulsive disorders, or microcephaly or mental retardation without serologic evidence of toxoplasmosis, while all children and adults, with central chorio-retinitis significantly show high dye test antibody titres, whether or not other signs of congenital toxoplasmosis are present.

It is the opinion of Fair and others that the commonest clinical form of congenital toxoplasmosis is that in which only the uveal structures are involved. A varying degree of mental deficit is usually detectable. Patients with life-long central chorio-retinitis are frequently accompanied by positive skin tests and dye tests of rather low antibody titres, e.g. 1:32, 1:64 and 1:128.

These are the very titres reported in visually defective and blind patients who suffer from recurrent attacks of toxoplasmic chorio-retinitis unassociated with other clinical signs. Similarly, low titres were also observed in patients from whose blind eyes viable parasites were isolated (Jacobs). It is further held that the eye is capable of harbouring active toxoplasmic lesions without evoking high dye-test antibody titres or that the titres, after an initial rise, quickly fall to a moderate level. Low dye-test titres are thus quite specific for ocular toxoplasmosis, and a small active uveitis within one or both eyes may suffice to give rise to a moderate increase in serum antibodies.

A survey of 686 mental defectives, aged sixteen and under, and of patients with a history of long-standing visual handicap, was conducted at Caswell Training School, Kinston, North Carolina, U.S.A., in April, 1958. The team was composed of a consultant ophthalmologist and the writer, using the skin toxoplasmin test, dye-test and ophthalmoscopic techniques. Five mental defectives, four females and one male, were detected as showing the signs of the congenital form of toxoplasmosis with pronounced chorio-retinal manifestations

Low dye-test titres and positive skin tests were obtained (Table I), and all patients had a history of defective vision of varying degrees; two patients had convulsive disorders of the major type and one showed intracranial calcifications of the diffuse, small circumscribed kind.

The five cases of congenital toxoplasmosis represent 0·7 per cent. of the 686 patients investigated and 0·25 per cent. of the total enrolment of 1930 patients resident at Caswell Training School.

TABLE I

Name	Case	Age	Sex	Skin Test Mothers	Skin Test Patients	Dye Test	Skull X-rays
Dorothy S. ..	1	37	F	+	+	+1:32	Small circumscribed areas of calcification throughout.
Frances H. ..	3	31	F	*	+	+1:128	No abnormal calcifications.
Mary C. ..	2	18	F	+	+	+1:64	No abnormal calcifications.
Brenda C. ..	4	12	F	+	+	+1:64	No abnormal calcifications.
Reginald G.	5	58	M	+	+	+1:64	No abnormal calcifications.

* Mother not available for skin test.

TABLE II

Name	No.	C.A.	I.Q. (Binet)	Vision	Epilepsy	Grade
Dorothy S. ..	1	37	48	Defective. Horizontal nystagmus internal squint (R.)	Major type	Mid-grade defective (imbecile)
Mary C. ..	2	18	70	Defective. Left external squint	None	High-grade defective Familial type (F.M.)
Frances H. ..	3	31	15	Almost blind in R. eye. Left eye removed	None	Low-grade defective microcephalic (Idiot)
Brenda C.	4	12	51	Very defective. Alternating internal squint	Major type	High-grade defective (F.M.)
Reginald G.	5	58	26	Grossly defective right cataract	None	Schizophrenia superimposed on mental deficiency, i.e. Pfropf-schizophrenia

CASE REPORTS

Case 1

Dorothy S., white, female, aged 37. History of grossly defective vision in both eyes. She is one of nine siblings (4th child); five are living and four dead. She is an epileptic of the major type. Father was an alcoholic and died of T.B. aged 33. Mother is still living and in good health. Parents were 2nd cousins. Patient had a record of backwardness at school.

Psychometric Test Data (Stanford-Binet):

26 January, 1928:	C.A. 6–11	M.A. 3–4	I.Q. 48
22 October, 1934:	C.A. 13– 8	M.A. 6–8	I.Q. 49
5 March, 1953:	C.A. 32	M.A. 7–2	I.Q. 48

Fundoscopic examination discloses tremendous bilateral chorio-retinal scars in each macula. In the right fundus is a large healed scar, strongly pigmented. There is bilateral horizontal nystagmus and internal strabismus involving the right eye.

Skull X-ray shows "small circumscribed areas of calcification throughout cerebral structures".

Patient's Skin Test (Toxoplasmin): Strongly positive.

Mother's Skin Test (Toxoplasmin): Positive.

Dye-Test (drawn, April, 1958): Positive, 1:32 (result received 10 December, 1958).

Diagnosis: Confirmed case of congenital toxoplasmosis in a mid-grade defective female, with major epilepsy.

Case II

Mary C., white, female, aged 18, familial type. Youngest of 3 siblings; birth weight 5½ pounds. No childhood illnesses. Gait awkward and history of defective vision. Mother is a mental defective of high-grade level, and maternal grandfather was defective too. Whilst imprisoned for murder, he died of cardiac disease at the age of 73. Maternal grandmother was also a high-grade defective and in poor general health.

Psychological Test Data (*Stanford-Binet*):

8 February, 1952: C.A. 12–8 M.A. 8–10 I.Q. 70
Bellevue-Wechsler Scale for Children: V.I.Q. 65 P.I.Q. 68 F.I.Q. 63

Fundoscopic examination reveals bilateral chorio-retinal scars, heavily pigmented. Anterior segment clear in each eye. Left external squint.

Skull X-ray is essentially negative.

Patient's Skin Test (Toxoplasmin): Strongly positive.

Mother's Skin Test (Toxoplasmin): Positive.

Dye-Test (drawn, April, 1958): Positive, 1:64 (result received 10 December, 1958).

Diagnosis: Confirmed case of congenital toxoplasmosis in a high-grade mental defective female (familial type).

Case III

Frances H., white, female, aged 31. Full-term 6 pounds baby; labour uneventful. During first 3 months there were prolonged fits of crying. She commenced teething at one year and walking at three years with some difficulty. She has never talked. Her right eye was removed prior to admission to Caswell Training School (9 December, 1949). She is almost blind now, stunted in growth, poorly proportioned and microcephalic (cranial circumference 16¾ inches). Her older brother is normal. Parental history is not available.

Examination of left fundus shows large central chorio-retinitis. Microphthalmia left eye. Right eye surgically removed.

Skull X-rays: Essentially negative.

Patient's Skin Test (Toxoplasmin): Positive.

Mother's Skin Test (Toxoplasmin): Not available for test.

Dye-Test (drawn 1 April, 1958): Positive, 1:128 (result received 10 December, 1958).

Diagnosis: This is a confirmed case of congenital toxoplasmosis in a low-grade microcephalic mental defective female, associated with microphthalmia (L) and almost complete blindness.

Case IV

Brenda C., white, female, aged 12, second of seven siblings. Walking began at 18 months and talking at two years. She had whooping cough (1948), chicken pox (1948), measles (1952) and mumps (1953). Since her early childhood, she has had a record of major epileptic seizures.

Father is in good health and of average intellectual ability. Mother is also normal.

Psychometric test (21 December, 1953) reveals C.A. 7–7, M.A. 3–10, I.Q. 51. Report adds that "patient shows extremely poor visual perception which cannot be improved with glasses".

Fundoscopic examination shows bilateral, central inactive chorio-retinitis. Each nerve head is quite pale but the vitreous body is clear. She also has alternating internal squint.

Skull X-rays: Essentially negative.

Patient's Skin Test (Toxoplasmin): Strongly positive.

Mother's Skin Test (Toxoplasmin): Positive.

Dye-Test (drawn 1 April, 1958): Positive 1:64 (result received 10 December, 1958).

Diagnosis: This is a confirmed case of toxoplasmosis in a high-grade defective female, with major epilepsy.

Case V

Reginald G., white, male, aged 58. He was considered mentally defective by his family but no detailed information is available regarding his developmental data except that he commenced walking at 2 years 3 months. He often expressed ideas that someone was out to harm him. He threatened on several occasions to commit suicide, and once he caught the coloured maid by the throat threatening to kill her. He gradually deteriorated, becoming temperamentally unstable and unmanageable. He is said to have set fire to a barn belonging to his parents when he was an adolescent. His father was a severe diabetic and the mother, who is still living, is in good health and mentally normal; a maternal aunt, however, was an epileptic suffering from major seizures.

Psychometric Test reveals (20 July, 1945) a C.A. 44–11, M.A. 2–6, and an I.Q. of 20, on the Kuhlmann Infant Scale. The psychologist further states "that the patient belongs to the

group of persons generally referred to as pseudo-mentally retarded, in view of his long history of delusions and hallucinations which are superimposed on a basic mental backwardness. In April, 1953, the patient's test data were C.A. 52–7, M.A. 4–1, I.Q. 26. The increase in the test score over the one obtained in 1945, is apparently an indication of a lessening of the intensity of the psychogenic disorder (Pfropfschizophrenia)".

Fundoscopic examination of right fundus "shows advanced cortical and nuclear cataract with no sign of old inflammation externally. The left lens is clear. There are a few small floating exudates in the vitreous humour and a large central chorio-retinal scar".

Skull X-rays "are essentially negative".

Patient's Skin Test (Toxoplasmin): Strongly positive.

Mother's Skin Test (Toxoplasmin): Positive.

Dye-test (drawn 1 April, 1958): Positive, 1:64 (result received 10 December, 1958).

Diagnosis: This is a confirmed case of congenital toxoplasmosis in a mid-grade mental defective male with superimposed schizophrenic psychosis described as Pfropfschizophrenia.

Summary

In a survey of 686 mental defectives, undertaken in April, 1958, by a consultant ophthalmologist and the writer at Caswell Training School, Kinston, N.C., comprising a total enrolment of 1,930 residents at the time of the study, five patients, four females and one male, were diagnosed as showing the clinical signs of congenital toxoplasmosis. Four patients had I.Q.s ranging from 15 to 70 points and one, being a case of chronic schizophrenia superimposed upon a condition of mental deficiency (Pfropfschizophrenia), an I.Q. of 26 points.

Intracranial calcifications were radiologically demonstrable in one patient (No. 1), and a history of major convulsions was recorded in cases No. 1 and No. 4. A history of visual handicap was reported in all patients, and a condition of cataract in the right eye was seen in case No. 5.

The skin toxoplasmin tests were positive in all of the five mental defectives and also in four of the patients' mothers; one mother, however, was not available for the skin test. The Sabin-Feldman methylene-blue dye test was positive in all patients, showing antibody titres ranging from 1:32, 1:64, to 1:128.

These low antibody titres were probably indicative of the large but localized toxoplasmotic lesions affecting the uveal structures primarily and to a lesser extent the smaller but more diffusely placed lesions in the central nervous and visceral systems.

In conclusion one may state that congenital toxoplasmosis is an important aetiological factor in the production of central, bilateral chorio-retinal lesions, and often the only clinical sign seen of the disease; it is also a pre-natal agency in the causation of mental deficiency of varying degrees and of developmental anomalies.

In addition one is right in saying that a mother, having borne one affected infant, develops such a degree of active immunity to toxoplasmosis that there is little risk of her bearing a second child similarly affected. Owing to the widespread distribution and frequency of toxoplasmosis in the normal population, attempts will have to be made to immunize previously uninfected pregnant mothers, in order to reduce the incidence of foetal infection and its undesirable consequences.

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