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Toxoplasmin sensitivity: subnormality and environment

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INTRODUCTION

There is some conflict of opinion regarding the importance of congenital toxoplasmosis as a cause of mental subnormality. Along with choroidoretinitis, hydrocephaly, microcephaly and convulsions, gross mental retardation is one of the classical signs of congenital toxoplasmosis, but the complete syndrome is extremely rare.

Thalhammer (1962) found that the incidence of positive dye test in grossly retarded infants without other signs of congenital toxoplasmosis was 20 % higher than that found in normal controls of the same age. He suggested that these children were suffering from what he termed 'oligosymptomatic toxoplasmosis'. More recently Remington (personal communication) claimed to have shown that a small but significant proportion of very young retarded children investigated by him owed their condition to toxoplasma infection. In contrast, Burkinshaw, Kirman & Sorsby (1953), Cooke & Derrick (1961), Fleck (1963) and Labzoffsky, Fish, Gyulai & Roughley (1965) all failed to find any evidence that toxoplasmosis was a significant cause of subnormality in the populations they studied. Although my dye-test survey of subnormals in hospital (Robertson, 1965) showed 20 % more positives among child defectives than among normal children the incidence was as high in mongols as in epileptics and other subnormals. Since the chromosomal anomaly responsible for mongoloid development seemed unlikely to be a result of protozoal infection, I concluded that the excess of dye-test positives among subnormal children was probably due to postnatally acquired infections and not to congenital disease. It seemed possible that as a result of some environmental or social factor severely subnormal children might be exposed to a greater risk of acquiring infection than were normal children.

The present investigation was undertaken in an attempt to locate such a factor.

Owing to the grave shortage of beds in the area it is difficult to secure early admission of defectives to hospital. If home care is possible subnormal children have to remain with their parents. Waiting-lists are very long, and can only be by-passed if home care is completely lacking or if serious behaviour problems render it impracticable. Consequently the children in hospitals for the subnormal are a highly selected group, many of whom were admitted for reasons similar to those which cause normal children to be taken into County Council children's homes. In order to see whether it was exposure to such conditions which had caused the high incidence of infection in the children in hospital I decided to test

a group of children admitted to children's homes in addition to a group of subnormals who were living with their parents and attending day training centres run by the County Council.

METHODS AND MATERIALS

Parental consent for a toxoplasmin skin-sensitivity test was sought in respect of all subnormals attending day training centres and in respect of children admitted to the children's homes run by the County Council of Lincoln, Parts of Lindsey. Those for whom consent was obtained were tested by intradermal injection of 0·1 ml. of an antigen supplied by Eli Lilly Inc., the antigen being a dilute sterile preparation made from peritoneal exudate of infected mice. The results were read on the third day, when an area of induration exceeding 7 mm. in diameter was read as a positive test.

The antigen and technique were the same as those used previously to survey subnormals residing in hospitals (Robertson, 1965).

RESULTS

The results of skin tests on subnormals under the age of 20 attending training centres and those in hospital are shown in Table 1. The total figures for patients under the age of 20 show the same incidence (12 in 120 = 10%) in training centre cases as that found among hospital cases (23 in 233 = 9·9%).

Table 1. *Toxoplasmin skin tests of subnormal patients*

	Hospital			Training centre			Total				
Age	No.	No. +ve	% +ve	No.	No. +ve	% +ve	No.	No. +ve	% +ve	S.E. of diff.	Diff./ S.E.
1–9	53	6	11·3	50	1	2·0	103	7	6·8	4·97	1·87
10–17	139	11	7·9	54	11	20·4	193	22	11·4	5·1	2·45
18–19	41	6	14·6	16	0	0·0	57	6	10·5	9·0	1·62
Total	233	23	9·9	120	12	10·0	353	35	9·9	—	—

The standard error of the difference in incidence between training centre cases under 10 years of age and those between 10 and 17 is 6·25, and diff./S.E. = 2·94.

The standard error of the difference in incidence between training centre cases aged 10–17 and those aged 18–19 is 10·0, and diff./S.E. = 2·04.

When the distribution by age is examined in greater detail, however, one finds that patients aged between 10 and 17 years attending training centres show a significantly higher incidence than do older or younger training-centre patients or hospital patients of the same age.

It seems likely that these differences may have resulted from selection. The most severely subnormal cases tend to remain insufficiently mature to attend training centres until after the age of 10, and either remain at home or enter hospital. They may attend training centres during their early 'teens' but are more likely than the higher-grade defectives to become unmanageable and require hospital care in late adolescence.

At the other end of the scale there are some children of higher intellectual ability who are educated in special schools up to the age of 16, but subsequently fail to adjust to employment, and are ascertained as subnormals and admitted to training centres at about the age of 18. The middle age range of training-centre patients would therefore tend to contain a higher proportion of low-grade patients than would the younger and older groups. A further selection factor could have resulted from the restriction of testing of training-centre patients to those whose parents consented, since consent given on admission permitted the testing of all the hospital patients.

Table 2. *Comparison of toxoplasmin skin sensitivity between subnormal and normal children in County Council care*

	Subnormals			Normal children in care			Total		
	No.	No. +ve	% +ve	No.	No. +ve	% +ve	No.	No. +ve	% +ve
1–9	103	7	6·8	19	0	0·0	122	7	5·75
10–17	193	22	11·4	52	1	1·9	245	23	9·4
Total	296	29	9·8	71	1	1·4	367	30	8·2

The standard error of the difference in incidence between all subnormals under 18 and all children in care was 3·62. Diff./S.E. = 2·32.

Table 3. *Toxoplasmin skin tests on mongols and other subnormals*

		Mongols			Other subnormals		
Age		No.	No. +ve	% +ve	No.	No. +ve	% +ve
1–9	Training centre	15	1	—	35	0	—
	Hospital	9	2	—	44	4	—
	Total	24	3	12·5	79	4	5·1
10–19	Training centre	23	1	—	47	10	—
	Hospital	26	3	—	154	14	—
	Total	49	4	8·2	201	24	12·5
20–29	Training centre	7	1	—	18	0	—
	Hospital	12	2	—	134	37	—
	Total	19	3	15·8	152	37	24·4
30–49	Training centre	4	0	—	10	1	—
	Hospital	19	3	—	267	82	—
	Total	23	3	13·1	277	83	30·0

Despite these differences, it was plain that the high incidence of positivity was not confined to the hospital patients, and the overall incidence of positive skin test was about 10% in both hospital and training-centre patients.

The incidence among children admitted to County Council children's homes was very much lower, only one out of 71 such children being positive. Since children only remain in County Council care up to the age of 18, the subnormals above that

age were excluded from the comparison made in Table 2. There were 29 positive reactors among the 296 subnormals under the age of 18, an incidence of 9·8 % compared with the 1·4 % incidence among normal children in care. As the standard error is 3·62 the difference between these two groups was just significant. Adverse home circumstances leading to admission to children's homes do not therefore lead to increased exposure to risk of toxoplasma infection, and the high incidence in young subnormals in hospital was related to the fact and severity of mental defect rather than to their home environment.

Combining the hospital and training-centre populations, it was possible to compare 115 mongols under the age of 50 with 709 other subnormals under the same age. These two groups are compared in Table 3, which shows quite clearly that in childhood the incidence of infection in mongols is at least as high as, and probably higher than, that in other subnormals. The incidence of positive skin test in mongols remains at about 11 % irrespective of age, but that in other subnormals rises from 5 % in those below the age of 10 to 30 % in those over the age of 30. The pattern among subnormals other than mongols is that of gradual acquisition of infection from continued environmental exposure to risk, and that among mongols is more consistent with congenital infection.

DISCUSSION

Hitherto most authorities have considered it unlikely that the chromosomal anomaly responsible for mongolism was a result of infection. The recent demonstration by Stoller & Collmann (1965) that peaks of incidence of mongol birth follow 9 months after epidemics of infective hepatitis, however, suggests the possibility that infection with this virus may cause trisomy. Jirovec, Jira, Fuchs & Peter (1957) in Prague found 79 out of 94 mothers of mongol children to be positive to the skin test for toxoplasmosis. The incidence varied from 81 % in mothers under the age of 30 to 94 % in those over the age of 40, figures far higher than those found in other women of the same age. The fathers of 39 of the mongol children were also tested but only 10 (26 %) were positive. In view of this evidence of an association between maternal toxoplasmin sensitivity and mongol births, the possibility that toxoplasma infection might interfere with meiotic cell division and produce trisomy cannot be dismissed. Toxoplasma, like the viruses, is an obligatory intracellular parasite, and could have similar effects upon cells. Unless the ovum itself contained parasites, however, one would not expect the children to be infected, and it seems unlikely that an infected ovum would develop into a viable foetus. Although there is evidence (Langer, 1963; Werner, Schmidtke & Thomascheck, 1963; Remington, Newell & Cavanaugh, 1964; Beattie, 1964; Robertson, 1966) that some chronically infected women may be liable to abort repeatedly, there is no evidence that live-born children of chronically infected mothers are congenitally infected. In France more than 83 % of the antenatal sera are positive to the dye test (Desmonts, Couvreur & Ben Rachid, 1965) and in England 25 % are positive, but in both countries sera of children over the age of 6 months are rarely positive to the dye test. Desmonts, Couvreur, Allison *et al.* (1965) found no positive reactors among

86 babies aged 6 to 11 months, and I found only 4 out of the 171 children below the age of 5 to be positive (Robertson, 1965). It would seem that children of women with low stable dye-test titres are seldom congenitally infected, and that even if toxoplasma infection of the mother were the cause of some cases of mongolism, infection of the mongol children themselves is probably acquired postnatally. The finding that subnormals, whether resident in their own homes or in hospital, show the same high incidence of postnatally acquired infection suggests that it may be some personal habit or pattern of behaviour more common among grossly retarded than among normal children which leads to an increased risk of infection.

Until the mode of transmission of toxoplasma has been determined the nature of this habit must remain in doubt. The results of recent experiments by Hutchison (1965) suggest one possible explanation. Hutchison succeeded in infecting mice with toxoplasma by feeding them with an extract from the faeces of a roundworm-infested cat, which had eaten toxoplasma cysts. The extract remained infective despite prolonged storage in tap water at room temperature, and he believes that the parasites were protected within the ova of the roundworm *Toxocara cati*. Garden soil is often contaminated with the faeces of dogs and cats. Since subnormals take longer than normal children to learn clean habits they may more frequently eat with, or suck, dirty fingers.

SUMMARY

The incidence of positive toxoplasmin skin test among subnormals in hospital was compared with that in subnormals attending day training centres and among normal children taken into County Council children's homes. Twelve out of 120 subnormals below the age of 20 attending day training centres were positive to the test, and 23 were positive out of 233 subnormals of the same age tested in hospital.

There was only 1 positive out of 71 children under the age of 18 in the County Council children's homes, compared with 29 out of 296 subnormals of this age who were tested.

The incidence of positive skin test among 115 mongols under the age of 50 was about 11% in each age range, whereas that in 709 other subnormals rose from 5% in those below the age of 10 to 30% in those over the age of 30.

Although factors similar to those causing admission of normal children to County Council care often determine the admission of subnormals to hospital, the children in County Council homes did not share the high incidence of infection which was found in subnormals.

It is suggested that the majority of infections among subnormal children are postnatally acquired. Since the incidence was the same in subnormals living at home as among those in hospital it is suggested that some personal habit commoner among subnormal than among normal children exposes the subnormals to an increased risk of infection.

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