feel that it is important to examine the stomach and duodenum carefully when clinical features such as we have described are encountered, since it may well be that these cases are less rare than a reading of the literature would suggest, and that this aspect of Crohn's disease has not received adequate attention.

The x-ray changes we have described are in our opinion characteristic. Further comment on the radiological findings may be made as follows: First, had the changes in Case 1 been confined to the stomach they might have been attributed to cancer of the diffusely infiltrating type (linitis plastica), but associated involvement of the duodenum and consideration of the age of the patient were of value in leading to a correct diagnosis. Secondly, the follow-up x-ray films of this case are also of interest in showing that the changes in the mucous membrane of the stomach and duodenum are not necessarily of a permanent nature, and that with the passage of time a return to a normal mucosal pattern is possible.

It should also be noted that both these patients became very ill on account of inability to assimilate adequate quantities of food. Case 2, which we have been able to observe in hospital, showed an upset in the protein content of the blood, and we feel it is important to stress the need for adequate dietetic care. Both these patients became anaemic, both appeared at one time to be going to die. A high-protein diet, as well as the prescribing of iron and vitamins, appears to us to be of importance in the handling of these cases.

Summary

Two cases of Crohn's disease involving the stomach and duodenum are reported; one of them was confirmed by biopsy of the gastric mucosa.

The radiological changes are described in detail.

We would like to thank Dr. H. S. Kellett for the pathological report and Mr. P. Harrison for the photographs.

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TOXOPLASMOSIS IN RELATION TO MENTAL DEFICIENCY

BY

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Mental deficiency is a social problem and does not constitute a clinical or pathological entity. On the contrary, it indicates a degree of mental retardation ranging from the near normal to a completely vegetative state. It is even less of a disease entity than is, for example, jaundice, and, like jaundice, it may be produced by a very large number of noxious agents.

The severer degrees of mental deficiency—that is, idiocy and imbecility—are now recognized to be always attended by cerebral lesions, often gross and obvious. The causes of these lesions are, however, far from obvious. The diagnosis of "primary amentia" is often made, though, as in other fields of medicine, the use of the word "primary" is a cloak for our ignorance of the aetiology.

In the absence of any specific medical treatment for mental deficiency interest in this field of medicine is

naturally concentrated on prevention, for which a knowledge of aetiology is essential. It is understandable, therefore, that whenever any new suggestion is made regarding the cause of even a few cases of mental deficiency it should be eagerly grasped at and explored by those working in this branch of medicine.

Toxoplasmosis as a cause of mental deficiency has been considered in America and on the continent of Europe. Accounts of the cerebral pathology are given by Wolf, Cowen, and Paige (1939) and by Gard *et al.* (1949). The clinical and pathological pictures vary considerably, but the introduction of reliable skin and serological tests has raised hopes of a more precise diagnosis.

The skin and serological tests were recently carried out by Dr. O. D. Fisher at the clinical laboratory of the Hospital for Sick Children, Great Ormond Street, on the entire population of a group of institutions for certified mental defectives, comprising 698 patients, made up of 623 children almost equally divided between the sexes, and 75 adult females. Details of the technical aspects of the testing, together with the results of the survey, were reported by Fisher (1951). As the present paper is complementary to Fisher's survey his findings are briefly summarized as follows:

All the patients were skin-tested, and those of the children who proved to be skin-positive to toxoplasmin had samples of venous blood examined serologically, using Sabin and Feldman's dye or cytoplasm modifying test. An excellent correspondence between the skin test and the serological reaction was obtained. Of the 698 patients tested, 55 showed dermal sensitivity to toxoplasmin (T-positive). Of these, 20 were female adults who did not have their serum tested. The remaining 35, who were children, were positive to the dye test. Of the skin positive children, 14 were boys and 21 girls. Twenty serological tests done on toxoplasmin-skin-test-negative patients were all negative. In 14 T-positive cases lumbar puncture was carried out. In none of these did the cerebrospinal fluid show any abnormality, and toxoplasmas were not found.

Present Investigation

In this investigation a note has been made of the percentage incidence of positive reactors in the different age groups of the 698 patients tested in Fisher's survey, and the 55 patients who showed positive toxoplasmin skin and dye reactions have been scrutinized clinically and radiologically for signs of toxoplasmosis.

Methods of Examination.—The scrutiny consisted in physical and ophthalmic examination and radiography of the skull. As a guide in the examination we used the criteria cited by Sabin (1948)—internal hydrocephalus or microcephaly; chorioretinitis with predilection for the macular region; convulsions and other signs of involvement of the nervous system; and cerebral calcification.

Results

Incidence of Positive Reactions.—The age distribution of patients who were positive is shown in Table I. These figures show a steady and significant rise in the proportion of positive reactions with age.

Physical Findings.—As all the patients examined were mentally defective it was to be expected that they would

TABLE I.—Incidence of Positive Toxoplasmin Reactions in Different Age Groups of 698 Mental Defectives

Ages:	0-4	5-9	10-14	15-19	20-24	25-29	30-39	40-49	50-60	Total
Total	65	246	192	108	29	16	13	17	12	698
Pos.	0	9	13	10	5	3	3	5	7	55
% Pos.	0	3.6	6.7	9.2	17.2	18.7	23.0	29.4	58.3	7.9

show certain non-specific physical abnormalities such as are commonly associated with the severer forms of mental defect—for example, dwarfing of stature, appearance of extreme youth, vascular stasis at the extremities. Moreover, many of the T-positive patients had been admitted to hospital with a recognized syndrome or obvious physical anomaly, and these would naturally show appropriate signs. The designation of the T-positive cases is shown in Table II.

TABLE II.—*Abnormalities Observed in Toxoplasmin-positive Cases*

Epilepsy	13	Microcephaly .. .	1	Strabismus .. .	5
Cerebral palsy and spastic diplegia ..	2	Epilepsia .. .	1	Deafness .. .	3
Hemiplegia .. .	5	Phenylketonuria ..	1	Psychotic features ..	2
Chorea .. .	1	Hydrocephalus .. .	1	Pleural effusion .. .	1
Mongolism .. .	2	Hypertelorism .. .	1	Kyphoscoliosis .. .	1
		Nystagmus .. .	4	Psoriasis .. .	1

Familial mental defect was noted in seven cases, and one case was the product of incest.

In carrying out the physical examination many abnormalities of this kind were found, but there was no frequently recurring pattern of physical signs to suggest that the cases had been subjected to the same pathogenic agent.

Degree of Mental Defect.—The distribution on the basis of intelligence tests of the T-positive cases is shown in Table III. The intelligence of T-positive patients varied

TABLE III.—*Degree of Mental Defect Observed in the 55 Toxoplasmin-positive Patients*

I.Q.	Classification	No.	%
0-20	Idiots	18	33
20-50	Imbeciles	27	49
50-70	Feeble-minded and educationally subnormal	4	7
70+	Within normal range	6	11

within wide limits from a vegetative idiot with an estimated "social quotient" of 2 up to a neurotic girl with an intelligence quotient of 104. The sample is overweighted with high-grade imbeciles by the fact that the older patients in the Fountain group are for administrative reasons mainly of that level.

Ophthalmological Findings.—The eyes of all the patients were examined. In 50 cases the examination included ophthalmoscopy. The results are shown in Table IV. Find-

TABLE IV.—*Ocular Anomalies Observed in 55 Toxoplasmin-positive Cases*

Cataract	2	Macular lesion with choroidal sclerosis .. .	1
Microphthalmos ..	5	One eye absent .. .	2
Corneal opacity ..	1		
Optic atrophy .. .	1		

ings similar to those regarded by Binkhorst (1948) as suggestive of toxoplasmosis were encountered in the eyes of only two patients. In one case there was a macular scar with calcareous dots in the right eye, and an associated temporal pallor of the disk; the left eye was normal. In the second case the appearances were less definite: in addition to a few dots scattered over both fundi, one fundus showed a reticular reaction temporal to the macula.

Radiological Findings.—Routine x-ray examination of the skulls of positive cases did not show any calcification which could be regarded as pathognomonic. In one instance, a case of tuberosc sclerosis, there was an appearance consistent with calcification of the glial nodules which is sometimes encountered in this condition. Four patients showed calcification of the pineal body. One patient had a cluster of opacities compatible with calcification in the choroid plexus of the lateral ventricle, another showed a small fleck of calcification in the temporal region, whilst in another there was a calcification of the falx cerebri. The only other case of radiological interest showed a striking and unusual picture of large plaques of calcification extending into the meninges within a hydrocephalic skull, particularly along the falx cerebri. This patient's deficiency was attributed by the parents to a fall down 20 steps at the age of 2. The radiological picture was compatible with calcification in an old subdural haematoma.

Discussion

The present findings show that positive skin and dye tests for toxoplasmosis are not uncommon in a population of mental defectives. However, this occurrence does not seem to be any more common in such patients than in the general population (Fisher, 1951). The incidence of positive reactions rises with increasing age in a like manner to other immune reactions—for example, the Schick test (Zingher, 1923, 1924). From this, and the absence in the clinical record of the positive patients of any illness which could be attributed to toxoplasmosis, it is suggested that the immune reaction is incidental.

In almost all our cases the mental deficiency was produced by factors operating before, at, or immediately after birth. But the figures presented suggest that the toxoplasmin-positive reaction is usually acquired some years after birth. It follows from this that toxoplasmosis is unlikely to be a frequent cause of mental deficiency.

It is known that some causes of gross brain damage operate only very infrequently. Thus in the population of the Fountain group at the present time (approximately 700) there are no cases definitely diagnosed as cerebromacular degeneration, Tay-Sachs's disease, or Schilder's disease, and only two with a diagnosis of gargoylism and one due to tuberculous meningitis. It may therefore be that, despite the negative conclusions drawn from the present investigation, toxoplasma does occasionally pass the placental barrier to produce a degree of brain damage compatible with survival of the infant.

It is clear that Binkhorst's assumption that positive serology confirms that abnormalities found in the patient—for example, hydrocephalus or microcephaly—are necessarily due to toxoplasmosis cannot be supported.

The results of the present survey do not permit any conclusions to be drawn on the possible incidence of a more acute form of toxoplasmosis which might prove fatal before admission to an institution for mental defect could be secured. A survey of toxoplasmin sensitivity in the mentally defective and the normal infant under 1 year might be helpful.

As to the origin of the positive reactions, if one assumes that the tests correlate with infection with actual toxoplasma there is no difficulty in explaining the exposure. Of the patients who have stayed in an institution for long periods of time, most have lived at home for varying periods, usually of several years. In that time they have had contact with cats and dogs, even though drawn from an urban area (principally that of the County of London in the case of our patients). Whilst in hospital contact with cats is common, since each ward has one or more cats. Two wards have canaries. A small "zoo" is kept within the hospital grounds. Despite all the efforts of the staff, periodic invasions of vermin—rats, mice, and beetles—occur. Furthermore, the ubiquitous sparrow leaves his droppings in all the playgrounds. Toxoplasma has been shown to live in a tremendous number of hosts, including dogs, rabbits, guinea-pigs, mice, rats, monkeys, pigeons, English sparrows, starlings, canaries, swallows, thrushes, chaffinches, and linnets. Also the organism has been found pathogenic for the cat, the pig, the shrew, the domestic hen (Wolf, Cowen, and Paige, 1939), and the hare in Denmark (Christiansen and Siim, 1951). Clearly the possibility of infection is widespread, but there is as yet little evidence to suggest that risk is worthy of special measures for its avoidance.

At different times the thesis has been advanced that mental defectives differ from the rest of the population in response to disease. In view of the gross cerebral pathology in idiots this might be thought likely, but there is no concrete evidence that immunological reactions are in fact different. On the contrary, the experience of this hospital in regard to the Schick test shows a normal response, as does the Mantoux reaction (Kirman, 1951). There is nothing in the present set of figures to suggest an abnormal response pattern to toxoplasmin in our hospital population.

Summary

The 55 toxoplasmin-positive patients found in a population of 698 mental defectives have been scrutinized for evidence of toxoplasmosis. Most of the patients were children. The incidence of positive cases increased with advancing age. In two cases eye lesions suggestive of toxoplasmosis were found. Radiology and lumbar puncture showed no findings suggestive of toxoplasmosis. In no cases could the mental defect be definitely attributed to toxoplasmosis. In some cases other definite causal factors were present—for example, epiloia, phenylketonuria, mongolism. It was concluded that in mental institutions or elsewhere a positive toxoplasmin reaction is acquired like a positive Schick reaction with increasing age, and is very infrequently associated with clinical toxoplasmosis; and that toxoplasmosis is not a common cause of mental defect.

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MYXOEDEMA AS A CAUSE OF DEATH REPORT OF TWO CASES

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Since the introduction of treatment with thyroid extract by Murray in 1891, it has been presumed that myxoedema as a cause of death is rare. We have been able to find only three recent references, and therefore report the following two cases.

Case 1

A woman aged 61 was admitted to hospital on January 7, 1951, with the following history. Thirty-five years ago she developed a left-sided hemiplegia, from which she made a good recovery. Two years ago she had another stroke, also involving the left side. Again recovery was fairly complete. The patient had had four children without trouble and the menopause had occurred at the age of 48. She had been in fairly good health until a fortnight before admission, when a cold and a severe cough developed. Her condition gradually deteriorated until January 6, when she first called in her doctor. He found her semi-conscious, and the following morning noticed considerable puffiness of the face.

On admission her pulse rate was 62 and temperature 97° F. (36.1° C.). She was moderately obese, and had pronounced supraclavicular fat pads. She was extremely lethargic but obeyed simple commands. Her voice was low-pitched and croaking. The scalp hair was dry and scanty, the pubic hair was extremely sparse, and the axillary hair was missing. Her skin felt dry and cold; her face, especially the eyelids, was puffy. Nothing abnormal was found in the heart, lungs, or abdomen. The blood pressure was 140/100 mm. Hg. There was pitting oedema of the legs up to the knees, and the hands were swollen but did not pit on pressure. Some evidence of previous hemiplegia was found in slight spasticity of the left side with an extensor plantar response, but there was no other abnormality in the central nervous system.

Investigations.—*Urine*: albumin was present; film showed scanty red cells, leucocytes, and mixed bacterial flora. The haemoglobin was 90%; blood urea, 50 mg. per 100 ml.; blood sugar, 57 mg. per 100 ml.; blood cholesterol, 390 mg. per 100 ml.; serum potassium, 18.4 mg. per 100 ml.; serum sodium, 345 mg. per 100 ml.; plasma chlorides, 595 mg. per 100 ml.; serum protein, total 7.2% (albumin 3.7%, globulin 3.5%, A/G ratio 1.1). An electrocardiogram showed flat and inverted T-waves in all leads, suggestive of myxoedema.

The diagnosis was difficult. Renal failure was suspected, but there was no confirmatory evidence on investigation. It was thought that an adrenal failure might be the cause, so treatment was started with penicillin and adrenal cortical extract, 10 ml. four-hourly. Although the patient became brighter mentally, her general condition deteriorated, respiration became laboured, and she died four days later. Her temperature remained at a low level all the time, and varied between 95 and 97° F. (35 and 36.1° C.). Her pulse rate varied between 60 and 70.

Necropsy

The following were the outstanding features: a widespread consolidation of the lungs; ante-mortem haemorrhages involving the suprarenals; remnants of thyroid gland; a heart of normal size and coronary vessels normal for her age.

Histological Examination.—Sections taken from both lobes of the thyroid gland showed marked fibrosis. A few small islets of lymphoid tissue were present in each lobe, and within these the remains of thyroid acini could be identified. The latter were composed of large pale irregular cells showing variable eosinophilic staining properties. Colloid was absent except in one small area. These remaining acini were surrounded by plasma cells and an outer zone of small lymphocytes. The *lungs* showed the picture of grey hepatization, with the alveoli distended by polymorphonuclear exudate. No heart-failure cells were present. *Kidneys*: the cortex was thinner than normal and patchy interstitial fibrosis was present. A considerable number of normal-looking glomeruli were to be seen. The vessels showed some thickening of the walls, but no elastosis.

Evidence of antemortem haemorrhage was found in the *suprarenal gland*. The *pituitary gland* was larger than normal. Acidophilic staining cells were noted to be extremely scanty, otherwise the histological appearance was within normal limits.

Case 2

An unmarried woman aged 50 was admitted to hospital on January 7, 1952. The previous history was that she had been well enough to do her own housework until five months before admission. Since then she had complained of weakness and of feeling cold, and these symptoms had gradually become worse. On the day of admission she suddenly complained of loss of vision, and the doctor found her lying across the bed unconscious.