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FREE CONTRIBUTIONS

First Group

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TAPETORETINAL DEGENERATION IN THREE MENTALLY RETARDED SISTERS WITH OTHER DISORDERS IN THE FAMILY TREE

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Three sisters suffering from tapetoretinal degeneration and other eye anomalies, mental retardation, skeletal abnormalities, and unusual dermatoglyphs, are reported.
The family tree of four generations is presented which reveals the following other disorders: diabetes mellitus (2 M), rheumatoid arthritis (2 F), mental retardation (2 M), congenital heart disease (1 F). A great niece of the propositi is known to suffer from tapetoretinal degeneration, mental retardation, epilepsy, cerebellar ataxia, and deafness. One miscarriage and one infant death are also noted.
The mode of inheritance and relationship to other syndromes with tapetoretinal degeneration are briefly discussed. The chromosomal studies, relevant biochemical and other investigations, are within normal limits.

INTRODUCTION

Tapetoretinal degeneration (TRD) — retinitis pigmentosa — can occur as an isolated abnormality (sometimes unilaterally), as a reaction to various infections, injuries or drugs, or as a concomitant of some hereditary degenerative syndromes and some inborn errors of metabolism whose manifestations may include severe neurological disorder.

Mental retardation has been reported in association with TRD in 4% of cases (Bell 1922), in 18% (Usher 1914), and in 25% in Hallgren's study (1959) of deafmutes. TRD and mental retardation are cardinal signs in such familial syndromes as that originally described by Laurence and Moon (1866).

A family with X-linked TRD was reported and linkage with Xg blood groups investigated by Klein et al. (1967).

A family was studied in which one sister suffered from TRD, severe mental retardation, deafness, psychotic episodes, dyskinesia with XX/XO chromosomes, and two brothers had defective sight and hearing, one of whom suffered from mutism (Jancar 1970).

We are presenting another family in which three sisters suffer from TRD, mental retardation, and physical anomalies, with normal female karyotypes and Xg (a+) blood groups. Other members of the family suffer from various disorders.

FAMILY HISTORY (Fig. 1)

The propositi are three sisters in a sibship of twelve; the ages of the mother and father at birth of the oldest sister were 23 and 29 years, respectively. Their father was married twice. There is no history of mental disorder or consanguinity on maternal or paternal side of the family. Their mother and one

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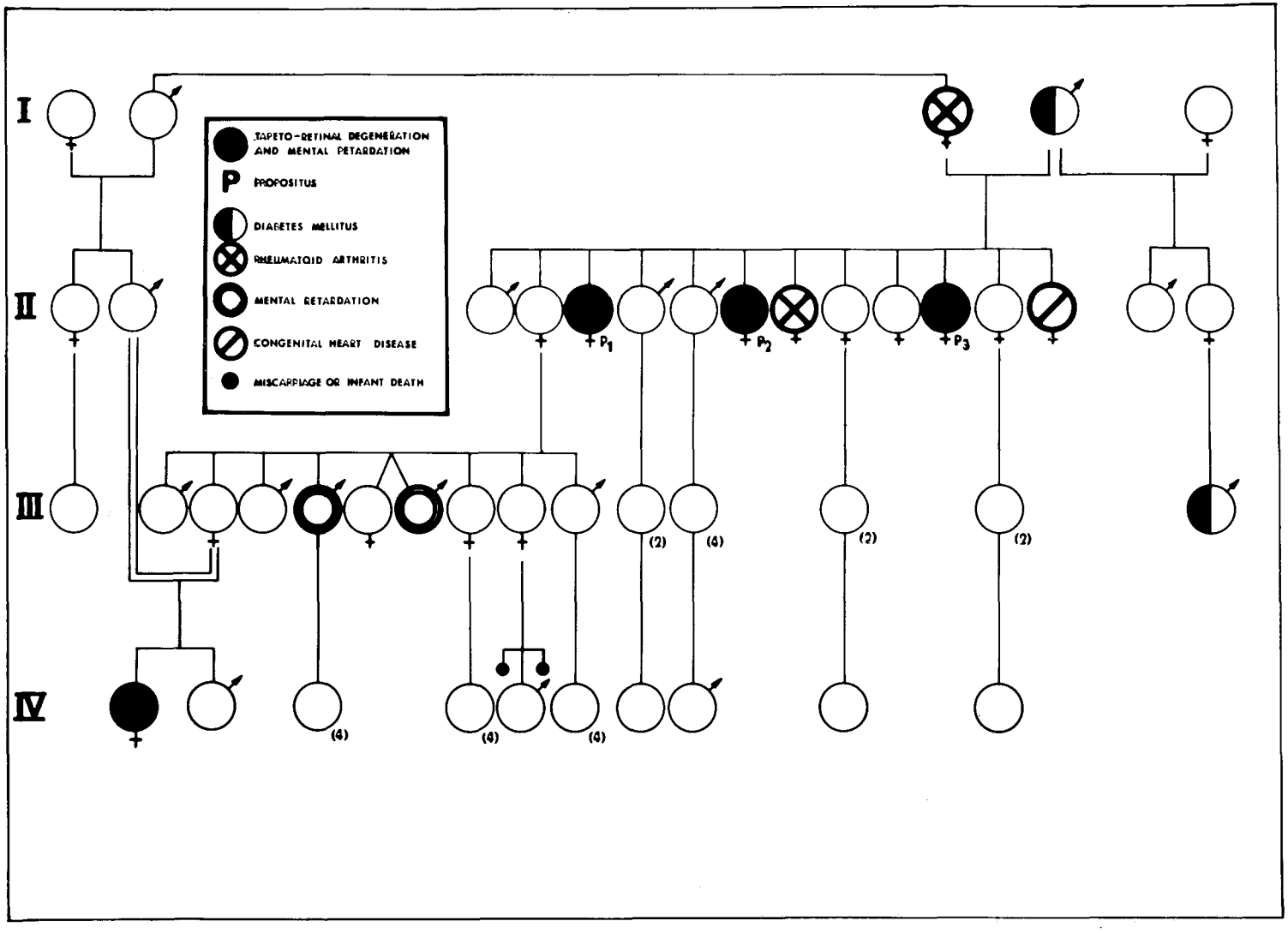

Fig. 1

sister suffered from rheumatoid arthritis, their father and his grandson suffered from diabetes mellitus. Their youngest sibling had a patent intraventricular septum and died during her first pregnancy of a subarachnoid haemorrhage. Two nephews are mentally retarded (IQ's 80 and 62). A great niece, examined at 5 years of age, suffers from TRD, bilateral optic atrophy, mental retardation, epilepsy, hypotonia, cerebellar ataxia, and deafness. The parents of this child are second cousins once removed. One miscarriage and one infant death are noted in the same generation.

CASE REPORTS

The patients were admitted to Stoke Park Hospital for the mentally retarded when aged 23, 16, and 18, respectively, and have remained there since.

Patient 1 (Fig. 2)

History. Ethel, born 1909. At age 25 she was noted to have pigmentary degeneration of the retina, hypermetropia, optic atrophy, scanty pubic hair, and infantile sexual development. At age 36 vision had reduced to hand movements only, and at age 38 bilateral cataracts and subacute glaucoma in the left eye were found. She was treated for the latter with trephining and iridectomy. At age 51 she was found to have a bilateral hearing loss, marked in the upper frequencies on the left.

Present condition. There is mild mental retardation (IQ 54); short stature (height 1.56 m, weight 53.5 Kg); microcephaly (skull circumference 52 cm). There is a coarse generalised intention tremor. Her eyes show a bilateral irregular pendular nystagmus, the right eye shows a marked lens opacity, and the left a hypermature cataract with a calcified mass at the upper pole, an inactive dilated pupil with marked atrophy and scarring of the iris. She is blind.

Patient 2 (Fig. 3)

History. Phyllis, born 1912. At age 29 she was noted to have poor sight with retinitis pigmentosa and optic atrophy and at 43 lens opacities were noted. At age 48 she was found to have a perceptive loss in upper tones in both ears at 1000 cycles per second with some scarring of both tympanic membranes. She has suffered from poor peripheral circulation and infections in her legs.

Present condition. There is moderate mental retardation (IQ 45), short stature (height 1.45 m, weight 46.7 Kg), microcephaly (skull circumference 49 cm); genu valgum, pes planus, kyphoscoliosis, clinodactyly of right little finger, and clino-camptodactyly of the left little finger. There is a mild tremor of the head and she is very frail. Her eyes show early lens changes with diffuse retinitis and dense pigment clumps at the periphery. She is blind.

Patient 3 (Fig. 4)

History. Lily, born 1918. High myopia and stippling of the fundi were noted at age 23, and at age 33 vitreous opacities, a small lens opacity on the right, and much myopic retinopathy were found. A left lens opacity was noted at age 35 and at age 42 retinitis pigmentosa.

Present condition. There is mild mental retardation (IQ 56), short stature (height 1.47 m, weight 48.5 Kg); microcephaly (skull circumference 51 cm), genu valgum, pes planus, and sluggish reflexes. Her eyes show a myopia requiring a correction of — 11.00 diopters in each eye. The fundi show a bilateral diffuse choroidal atrophy with fine pigment deposition and proliferation of the retinal pigmented epithelium, the peri-macula being spared. Hearing is normal. Skull X-ray shows a fine reticular shadowing involving the calvarium.

All three patients have generalised fine translucent skin with prominent venous marking. Cafe-au-lait spots and leucodermic patches occur over trunk and arms and on the exposed parts of the body there is increased patchy pigmentation.

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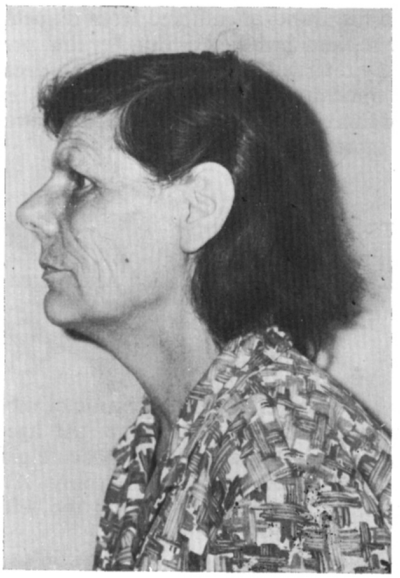

Fig. 2. Patient 1

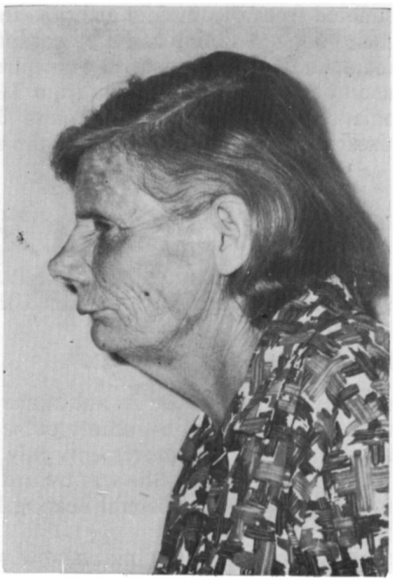

Fig. 3. Patient 2

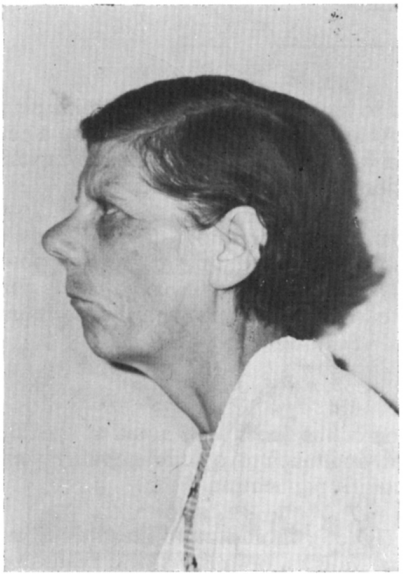

Fig. 4. Patient 3

THE THREE MENTALLY RETARDED SISTERS WITH TAPETORETINAL DEGENERATION

In all three patients blood count, W.R. and Kahn, serum cholesterol and lipoproteins, gas-liquid chromatography, urinary mucopolysaccharides, aminoacid chromatography and 17 Keto-steroids, and EEG's, are within the normal range. Dermatoglyphs of all three patients showed very unusual finger and toe prints with a large number of lateral pocket loops, the significance of which is unknown.

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DISCUSSION

Sorsby (1970) suggests four or more modes of inheritance of TRD with different genes responsible: recessive, dominant, sex-linked recessive, partial or intermediate sex-linkage. Klein et al. (1967) found in 90% of cases that the mode of inheritance was by an autosomal recessive gene. The disorder described in our patients appears to be inherited as autosomal recessive, a conclusion supported by the more severe condition in the great niece, whose parents are second cousins. It seems probable that the same genetic defect is responsible in all four cases.

The fact that two of our patients and their niece suffer from deafness suggests that they should be linked with such syndromes as Hallgren's, Cockayne's, or Alström's. The latter two syndromes do not show neurological abnormalities and our patients may be variants allied to these syndromes, the hereditary degenerative syndromes of CNS with TRD and syndromes such as the Laurence-Moon-Biedl with TRD, skeletal abnormalities and hypogenitalism. Diabetes mellitus has been reported in Alström's cases, in Refsum's disease (Heycock and Wilson 1958), in the Laurence-Moon-Biedl syndrome, and frequently in Friedreich's ataxia (Ashby and Tweedy 1953).

Other cases with TRD, mental retardation and various anomalies are recorded in the literature (François and Descamps 1951, McKusick et al. 1966, Quarcoopome 1970, Mirhosseini et al. 1972).

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