Discussion

In these two patients we have established monozygosity as well as concordance for xerodermic idiocy by most of the accepted standards used at the present time. Zygoty was determined by similarities in physical appearance, the blood groups, and dermatoglyphics. Concordance for the neurological features appeared to be incomplete, but this may be due to the difference in the rate of progress of the disease, as had been noted in a large series of patients by El-Hefnawi, El-Nabawi, and Rasheed (1962). A mutant gene of large effect is suggested as the cause of the disease by its occurrence in identical twins.

For the twins to have inherited an autosomal recessive condition, both parents must be heterozygous carriers of the mutant gene. Although there are reports suggesting that freckling is seen in heterozygotes (Cockayne, 1933), the parents did not show any clinical evidence of the disease. In the large series reported from Egypt (El-Hefnawi *et al*, 1962) consanguinity was found in most of the families, but the parents of our twins were unrelated and this was not surprising as consanguineous marriage is rare in the Malaysian Chinese.

The twins appear to have both cerebral and cerebellar damage and this corresponds with the post-mortem findings in a patient reported by Reed *et al* (1969). The neurological manifestations are marked, but the twins have not developed cutaneous malignancy, a hallmark of xerodermic idiocy. The precautions taken by the mother after their early exposure on the beach and the semi-bedridden state of the patients may have diminished their exposure to sun light, the ultra-violet rays of which are the chief exciting agent for the development of cutaneous malignancy. The neurological features, the mechanism of which is not understood at present, are probably not dependent on the damaging effects of ultra-violet irradiation. Attempts have been made to explain the manifestations of the disease by biochemical defects, but the investigations were essentially normal in our patients, as they have been in most publications.

Cleaver (1968) demonstrated *in vitro* that DNA repair replication after ultra-violet irradiation is absent or reduced in the fibroblasts from patients with xeroderma pigmentosum compared with normal controls. Epstein *et al* (1970) showed the same defect in the epidermal cells of the skin *in vivo* and the defect was more marked in xerodermic idiocy than in individuals without neurological manifestations. However, a relationship between the development of cutaneous malignancy and defective DNA synthesis has yet to be established

Weerd-Kastelein, Keijzer, and Bootsma (1972) have proposed that xerodermic idiocy and classical xeroderma pigmentosum are caused by two different genes.

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Progeria in twins

Summary. A pair of male monozygotic twins, both affected by progeria is described. The concordance in this manifestation suggests a genetic aetiology and other evidence indicates the implication of autosomal recessive factors; the chromosomes of these patients show no detectable abnormalities.

Progeria (Hutchinson-Gilford progeria syndrome) is a very rare condition, its incidence being estimated as 1 per 8,000,000 births (de Busk, 1972). It is characterized by symptoms that mimic premature ageing, death generally occurring before 20 years of age. About 60 patients have been described so far. We present here what is believed to be the first observation of progeria in twins.

Case reports

The twins are male and both are affected (Fig. 1). They were born at Piratini, RS, Brazil, the product of the 10th gestation of a mulatto woman; at delivery she was 33. Their father, also a mulatto and not biologically related to his wife, was 38 years old at the time of their birth. Both parents are normal, as are their 13 other offspring: six boys and five girls plus a dizygous pair of twins. There is no family history of premature ageing, alopecia, or severe growth failure.

The propositi were referred to the Departamento de Pediatria of the Universidade Católica de Pelotas, RS, Brazil and were hospitalized at the age of 7 because of poor weight gain and open anterior fontanelles. At that time their heights were 96 cm (twin 1) and 95 cm (twin 2), both weighed 12.5 kg. Their crania were large in relation to their faces, with a circumference of 51 cm, and they also showed prominent scalp veins. Despite their markedly hypotrophic muscles their activity was normal; a 'horse-riding' stance was noticeable. Subcutaneous fat was almost absent. The anterior fontanelle measured 2×2 cm on both twins and they had only sparse, short, thin hair, restricted to the occipital region. Eyebrows were absent and the eyelashes were few and sparse. Ophthalmoscopy revealed a slightly increased tortuosity of the vessels. Their noses and ears were small, the latter being quite sensitive to touch and having a wide diameter of the external canal. The temporary dentition was complete, with maloccluded teeth; micrognathia and arched palate were present. Both twins had an enlarged abdomen, the liver being palpable 2 cm below the midcostal margin. The external genitalia appeared normal. The limbs were thin with prominent knees and elbows; joint stiffness occurred with limitation of movements especially of the hands. The skin was dry, thin, with an aged appearance mainly on their hands and feet. Toes and fingernails were markedly dystrophic. They showed poor adaptation to the hospital conditions and psychological studies indicated that they were severely depressed; their IQs, however, were normal.

FIG. 1. Frontal view of the patients aged 7.

A series of biochemical blood and urine determinations were essentially normal, as were the thyroid function studies, ECG, EEG, and audiometric tests. Radiology showed marked hypoplasia of facial bones with abnormal craniofacial proportions, patent anterior fontanelles, thin and hypoplastic clavicles with resorption areas at both extremities, and bilateral coxa valga.

Their chromosomes were normal. Both of them showed the following blood groups: O, MNSs, CcDEe, Fy(a+), K(-), k(+), P(+); haptoglobin type: 1-1.

Dermatoglyphics were as follows: twin 1:—left hand: whorl (W), W, W, ulnar loop (L^u), L^u ; right hand: W, W, L^u , L^u , L^u . Twin 2:—left hand: W, W, W, L^u , L^u ; right hand: W, W, W, L^u , L^u . Palmar features of twin 1 showed an *ab* count of 75; *atd* angle of 83°, and an abortive simian crease on the right hand. Twin 2 had an *ab* count of 76; *atd* angle 87°, and a bilateral simian crease. Using the genetic markers indicated above and the *atd* angle we arrived at a probability of only 1.9% that they were dizygotic.

Discussion

Only two other typical cases of progeria have been reported from Brazil (de Souza, 1968; Mar-

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condes *et al.*, 1969). As is true for the great majority of patients described, they were sporadic; no other affected members being known in their families. Only four instances of familial cases are known to us. Consanguinity, however, has been found in three out of 19 families in which it was sought, a strong evidence in favour of recessive genes being implicated in the aetiology of this disease. Cell culture investigations support this conclusion (Danes, 1971). The concordance in the manifestation of this condition in our pair of monozygotic twins is another indication that it could be due to genetic factors. Accepting this hypothesis, the probability of obtaining the extreme segregation ratio observed in our sibship (one affected zygote in 14) is 8.4%. In accordance with previous observations (*cf.* Macnamara *et al.*, 1970; de Busk, 1972) the chromosomes of our patients showed no detectable abnormalities.

Several authors stressed that the ears of persons with this disease tend to protrude and that the lobes are frequently absent. Our patients, in addition, have very wide external canals that permit the observation of the tympanic membrane without special light. This exaggerated diameter of the auditory external canal was also present in de Busk's case 60 (1972) and probably should be considered as a possible sign in future descriptions of this condition.

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21 Monosomy in a retarded female infant*

Summary. A 20-month-old female infant with complete monosomy 21 is described. She has marked mental and physical retardation, antimongoloid slant, low set ears, micrognathia, syndactyly of the toes, and cardiac abnormalities. Karyotypes of fibroblasts and lymphocytes, examined with Giemsa banding, quinacrine banding, and reversed banding techniques revealed no evidence of translocation.

The application of chromosome banding techniques in cases of apparent complete G monosomy has revealed that most have a translocation involving chromosomes No. 21 or No. 22, or mosaicism with one 45,–21 cell line (Wyandt *et al.*, 1971; Cooksley, Firouz-Abadi, and Wallace, 1973; Richmond, MacArthur, and Hunter, 1973). One case has been reported in which absence of one chromosome 21 has been documented by banding techniques (Gripenberg, Elfving, and Gripenberg, 1972). We report here a case of apparent monosomy 21 in a 20-month-old female infant.

Case report

The patient, a 20-month-old female, was the first child of a 23-year-old mother and a 25-year-old father. The parents are not related. A paternal uncle is reported to be retarded.

The child was born at 38 weeks' gestation following a pregnancy complicated by emotional and social problems in an unwed mother for whom there was no prenatal care. Delivery was normal and the baby weighed 1900 g and had a length of 46 cm. She had several generalized seizures during the first few days of life which were interpreted as secondary to hypoglycaemia and responded to therapy with glucose. At 3 weeks of age, evaluation of failure to thrive revealed absence of a G-group chromosome. Subsequently the child continued to show re-

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