amplification using a modified primer on the 5’ side of codon 542 and subsequent digestion with RNase H. The mutation (G→T c.1756) was characterised by direct sequencing using the Sequenase USB kit by standard methods. G542 is a nonsense mutation in which a glycine at codon 542 is replaced with a stop codon G542X in the cystic fibrosis transmembrane conductance regulator gene. This boy has a severe lung involvement, meconium ileus, and pancreatic insufficiency, as indicated by the high degree of statorrhoea. The G542 nonsense mutation was associated with a severe clinical phenotype in the neonatal period.

This case shows that, in contrast to earlier reports, the G542 nonsense mutation alone, which truncates the gene product to 37% of its length, may lead to severe cystic fibrosis. The explanation for these conflicting results may be resolved by RNA studies. Nevertheless, a severe phenotype in the neonatal period may change with age to a moderate phenotype and vice versa. Environmental, epigenetic, and therapeutic factors can influence the clinical course. Furthermore, it is difficult to predict the severity of the disease. This case illustrates again that the presence of any specific CFTR mutation offers little in the way of a prognostic indicator in the individual patient.

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Cutis laxa and the Costello syndrome

We reported a series of children with cutis laxa in this Journal in 1987.1 Prompted by a recent article by Kalouzian et al2 on the Costello syndrome, and concerns that our case had some atypical features of cutis laxa, we have taken the opportunity to review this child and found she has now developed nasal lax skin and clearly has the Costello syndrome. This syndrome was originally described by Costello in the Australian Paediatric Journal in 1977.3 The author described two unrelated children with growth and developmental delay together with lax skin and the onset of nasal papillomata in the first decade of life. Two further cases of the syndrome have been reported subsequently.4,5 Since it remains a rare but very characteristic syndrome we would like to update our original case report.

The proband was originally seen when she was 2½ years of age. At that time the coarse facial features and loose skin had suggested a diagnosis of cutis laxa (fig 1). A subsequent skin biopsy showed that the elastic fibres were normal on histological examination, but there was a relative deficiency of well formed collagen fibres. Her development has continued to be considerably delayed. She walked at 5 years and has received special education. Feeding has remained a problem, although no anatomical or physiological abnormality has been specifically identified. She was treated with growth hormone from 4 years of age and at 10 years her height is 118.5 cm (<3rd centile). She has always been relatively macrocephalic (head circumference has been on the 25th centile) and her anterior fontanelle was late in closing. Her facial features have been relatively coarse with a flat nasal bridge, hypertelorism, downward slanting palpebral fissures, a short neck, and a barrel shaped chest. She has a moderate lumbothoracic scoliosis with limitation of movement at the knees and elbows. There is pes planus with a tendency to walk with the feet in an everted position.

At 6 years of age she developed nasal warts which have tended to recur in spite of aggressive treatment using cryosurgery. She has no warts elsewhere and she has no adverse reaction to other viral infections. Her routine immunological parameters are normal. Although she is of West Indian origin, her skin is considerably darker than the other members of her family especially over the dorsum of her hands. Hyperpigmentation has also been reported in previous cases of Caucasian origin. One of the striking features which distinguishes this syndrome from other causes of cutis laxa is the deep palmar creases and thickened dermal ridges which have an unusual ‘velvety’ feel (fig 2).

All cases of Costello syndrome have been isolated cases. In this family the parents have had a further unaffected son since the original report. The inheritance pattern therefore remains unclear.

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4 Santos HG. Costello syndrome: another case. European Society of Human Genetics, Denmark, 1992, Abst 251.

Figure 1 Patient at 2 years of age when reported as an example of cutis laxa. Note the lax skin is most marked over the hands and feet. There is short stature and relative macrocephaly.

Figure 2 The dermal creases are very marked and the palms of the hands are ‘velvety’ to feel. This feature was present from an early stage before the nasal papillomata developed and is a useful sign to distinguish the Costello syndrome from other causes of cutis laxa.
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