Fig. 3 Deficiency in elastin in conducting pulmonary artery branch. (Elastin Van Gieson $\times 100$).

mental and physical deterioration, leaving unfulfilled the hopes previously expressed by Walker-Smith *et al.* (1973) and Grover and Scrutton (1975).

Summary

In an infant with Menkes's steely-hair syndrome, early treatment (from 21 days of age) with parenteral copper failed to halt the disease. In addition to urinary tract abnormalities, panlobular emphysema was present, a finding not previously noted in the syndrome.

We thank Dr Delves, The Institute of Child Health, London for measurement of serial copper and ceruloplasmin levels.

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Use of salbutamol powder in childhood asthma

It has now been established that salbutamol, delivered as a nebulised solution, is effective in reducing acute airways obstruction in children older than 20 months with recurrent wheezing episodes (Lenney and Milner, 1978). It is also accepted that this form of treatment is at least as effective as intravenous therapy in relieving the severe acute asthmatic attack (Godfrey, 1977) and, unlike oral preparations, blocks exercise-induced bronchoconstriction (Anderson *et al.*, 1976). Unfortunately nebulising

systems are cumbersome and relatively expensive. In the older child pressurised bronchodilator aerosols are effective in producing rapid relief of airways obstruction (Hambleton and Shinebourne, 1970). However, children less than 6 years are rarely able to manage the pressurised aerosols successfully and when asthma is severe in this age group oral bronchodilators are usually ineffective. Fluorocarbon compounds used as propellants in pressurised aerosols have been shown to induce ventricular arrhythmias in animals (Clark and Tinston, 1972) and to reduce the amounts of ozone in the stratosphere (Molina and Rowland, 1974).

Salbutamol is now available in dry powder form in a capsule, the powder being inhaled through a specially designed 'rotahaler'. We have found that children younger than 5 years can manage the rotahaler successfully and therefore salbutamol powder may be a useful addition to the treatment of asthma.

Salbutamol powder and salbutamol aerosol in the older asthmatic child

Patients. Ten children (5 boys and 5 girls) took part in the initial study to compare salbutamol powder with salbutamol aerosol. Their ages ranged from 6 to 13 years. They all suffered from chronic asthma and were taking bronchodilators regularly. Three children were also receiving sodium cromoglycate and three beclomethasone dipropionate.

Method. The children were given an Airmed peak flow gauge to take home and at 5 p.m. each day for 21 days peak expiratory flow rates (PEFRs) were recorded. They then inhaled 200 µg salbutamol powder and PEFRs were recorded 10 min later.

200 µg salbutamol aerosol were then inhaled and PEFRs again recorded after a further 10 min. All recorded PEFRs were the best of three attempts. The children received their regular treatment as usual but none was given in the 4 hours before 5 p.m. on any day. The protocol was repeated for a further 21 days but this time the aerosol was administered before the powder.

Results.

Days 1–21. The mean increase in PEFR after powder was 20.2% (range 8.4 to 42.6%) and a further mean increase in PEFR of 6.6% (range 1.9 to 19.3%) occurred after aerosol administration.

Days 22–42. The mean increase in PEFR after aerosol was 14.7% (range 3.7 to 26.8%) and a further mean increase in PEFR of 10.4% (range 2.4 to 23.4%) occurred after powder. These results have also been expressed as the mean percentage PEFR of the predicted value for each patient (Table 1).

Discussion. The baseline mean PEFRs for the two 21-day periods were not statistically significantly different. Both forms of treatment produced useful but submaximal bronchodilatation. These results indicated that the powder was at least as effective as the aerosol in this age group. Similar results have been found in adults (Hetzel and Clark, 1977).

As we were concerned about a placebo reaction we also studied another 7 asthmatic children on two occasions within 14 days. Their ages ranged from 5 to 10 years (5 boys and 2 girls). All children were wheezing at the time of study; baseline PEFRs were obtained; the children were then given either placebo powder or salbutamol powder under double-blind

Table 1 Mean percentage of predicted PEFRs in 10 children, initially, 10 min after salbutamol powder, and 10 min after salbutamol aerosol in two consecutive treatment periods of 21 days each. In the 1st period salbutamol powder was given before salbutamol aerosol and in the 2nd the treatment order was reversed

Age of patients (years)	Treatment period (days 1–21)			Treatment period (days 22–42)		
	Initial mean PEFR (% predicted)	Mean PEFR 10 min after salbutamol		Initial mean PEFR (% predicted)	Mean PEFR 10 min after salbutamol	
		Powder (% predicted)	Aerosol (% predicted)		Aerosol (% predicted)	Powder (% predicted)
6.2	39	52	54	50	61	70
9.4	45	63	67	54	62.5	72
10.1	88	97	99	75	95	98
10.9	85	97	102.5	74	85	92
10.3	78	89	91	74	88	101
11.6	56	68	76	52.5	66.5	76
12.5	56.5	69.5	71	68.5	78	80
13.1	72	85.5	91	91.5	100	102
13.4	66	73	87	66	78	88
13.8	70	82	86	72	80	86
Mean						
11.3	65	77.5	82.5	67.5	79.5	87

conditions and the PEFR was recorded 10 minutes later. The mean increase in PEFR after placebo powder was 3.7% (range 0 to 10%) and the mean increase in PEFR after salbutamol powder was 55% (range 30 to 137.5%).

The results of this small study indicate that the response to salbutamol powder was not a placebo reaction.

Salbutamol powder in the young asthmatic child

The second part of the study to determine the effect of salbutamol powder in asthmatic children younger than 5 years, was carried out in the paediatric outpatient departments at Nottingham Children's Hospital and Nottingham City Hospital.

Patients. Fourteen children (9 boys and 5 girls) took part in the study. Their ages ranged from 3 years to 4 years 10 months. At the time of study they all had expiratory rhonchi and were considered to have childhood asthma. All had previously received bronchodilator treatment with apparent clinical improvement in their symptoms. Seven had a previous history of eczema and 9 had a family history of asthma, eczema, or hay fever in first-degree relatives.

Method. PEFR was measured using the Wright low range peak flow meter. As previously, the best of three blows was recorded. The children then inhaled 200 µg salbutamol powder using the rotahaler and PEFRs were remeasured 10 min later.

Results. None of the children had previously used the rotahaler and although they all managed it satisfactorily, the younger ones sometimes required more than one inhalation to empty the capsule of powder completely.

Table 2 *Percentage predicted PEFRs in 14 young children, initially, and 10 min after inhalation of salbutamol powder*

<i>Ages of patients (years)</i>	<i>Initial PEFR (% predicted)</i>	<i>PEFR 10 min after salbutamol powder (% predicted)</i>
3.0	80	90
3.1	85	98
3.8	67	90
3.9	71	104
4.0	80	89
4.1	73	91
4.1	67	85
4.2	56	74
4.5	70	96
4.6	85	92
4.7	75	96.5
4.8	88	100
4.8	78	89
4.9	81	95
Mean		
4.17	75.5	92

Table 2 shows the initial PEFRs and the PEFRs after the 14 children had inhaled the salbutamol powder, expressed as a percentage of the predicted value (Milner and Ingram, 1970). The mean absolute increase in PEFRs after the salbutamol powder was 22.5% (range 8 to 42%). The two youngest children (aged 3 years and 3 years one month) showed absolute increases in PEFR of 12.5 and 13.5% respectively.

Discussion

This study shows that, in the older child, salbutamol powder is as effective as salbutamol pressurised aerosol. Under age 7 years, children do not co-ordinate sufficiently well to obtain maximum benefit from the pressurised aerosol systems. Nebulised salbutamol in this young age group is effective but the system is relatively expensive and only suitable for use within the home. We found that children aged 3 years can use the rotahaler device satisfactorily, and even at this age do obtain some relief, although to a lesser extent than that obtained by older children. We conclude that this is a useful addition to currently available forms of treatment in young children with asthma.

Summary

In this study on 31 asthmatic children, salbutamol powder was as effective as salbutamol aerosol in the older asthmatic child studied daily during a 6-week period. The rotahaler can be used successfully from 3 years and, as measured by the peak expiratory flow rate, salbutamol powder is effective in this young age group.

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Depigmented hair

The earliest sign of tuberous sclerosis

Tuberous sclerosis is an important cause of infantile spasms or other early epileptic seizures with developmental delay—that is, of seizures suggesting an underlying cerebral malformation. Diagnosis is necessary to allow appropriate management including precise genetic counselling. Until now the earliest useful external sign has been the ash-leaf shaped depigmented macule or 'white spot'. Unfortunately these depigmented macules are not always visible at birth or in early months of life, particularly in fair-skinned individuals or in the absence of sun-tan.

We recently observed 4 children with tuberous sclerosis each one of whom had had at least one tuft of white scalp hair present since birth. This sign is illustrated in an encyclopaedic textbook (Swaiman and Wright, 1975). Patches of grey (poliosis) or white (leukotrichia) hair are common in tuberous sclerosis and were present in 18% of cases in a survey from hospitals for mental deficient patients (Nickel and Reed, 1962). However this is not generally recognised by paediatricians and the sign received no mention in a review of 100 affected children (Pampiglione and Moynahan, 1976). No previous

paper has drawn attention to this distinctive feature as the earliest sign of the disorder.

Patients

The children reported all attended this hospital during 1977. They had originally presented with developmental delay and with either infantile spasms or other varieties of epileptic seizure, suggestive of an abnormally structured brain. The parents of each child had noticed one or more patches of white hair soon after birth (Figure) but had not observed other stigmata of the disease until much later (Table). Case 1 was the only infant to be seen by one of us at an age when depigmented hair was present but no characteristic depigmented macules were detectable even though these were sought; 13 months later depigmented macules had appeared where initial colour photographs confirmed their previous absence.

We could not recognise any depigmentation of the scalp underlying the white tufts, nor did we make any biopsies, but in Case 3 one tuft abutted the temporal hair line and clearly arose from the continuation of an ovate, depigmented macule on the adjacent hairless skin (Figure).

Discussion

Tuberous sclerosis is an important cause of early seizures with impaired development and on follow-up accounts for at least 25% of cases of infantile spasms (Pampiglione and Pugh, 1975). The early diagnosis of tuberous sclerosis has been much easier since it has been known that ash-leaf shaped, depigmented macules are characteristic of the disorder (Gold and Freeman 1965; Fois *et al.*, 1973) and are probably present at birth (Fitzpatrick *et al.*, 1968). However, these white macules may not be visible in fair-skinned infants, even under Wood's light, and may not become apparent until solar pigmentation is acquired (as may have been the case in Case 1).

Depigmented hair does not have this disadvantage, being readily recognised, if looked for, even in the

Table Four children with tuberous sclerosis, presenting with early seizure and developmental delay, in whom a tuft of white hair had been present since birth

Case	Age (months)			Other manifestations of tuberous sclerosis
	At presentation	At diagnosis	At which white macules noted	
1	5	18	18*	Epilepsy, mental retardation, shagreen patch
2	5	8	8	Epilepsy, retinal phakomata
3	2	84	24	Epilepsy, mental retardation, adenoma sebaceum
4	18	84	24	Epilepsy, mental retardation, adenoma sebaceum

*Not present at 5 months.