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Incidence of growth hormone deficiency

Growth hormone for therapeutic purposes is extracted from human pituitaries. It is of value to those responsible for its preparation to know the approximate incidence of the only conditions for which it is of value, idiopathic growth hormone deficiency and growth hormone deficiency secondary to intracranial disease. This paper explores the evidence about this from the Newcastle upon Tyne region.

Evidence

Growth clinic patients. Since 1967 a clinic has been held at the Royal Victoria Infirmary at which patients from the Newcastle region requiring growth hormone have been seen regularly. As the major centres of population in the region are separated from other reference hospitals by long distances and large tracts of sparsely populated country, it is likely that these patients comprise all those in the region known to have growth hormone deficiency.

The patients discussed in this paper have all been diagnosed as being deficient in growth hormone on the basis of low serum growth hormone levels after an adequate hypoglycaemic stimulus, and have been accepted into the Medical Research Council growth hormone treatment trial. Children with psychosocial dwarfism associated with low serum growth hormone levels and other short patients who are not growth hormone deficient but who have been given a trial of growth hormone, e.g. those with Silver's syndrome, have not been included.

Altogether there have been 21 patients of this type, 12 with idiopathic growth hormone deficiency (9 males and 3 females) and 9 (3 males and 6 females) with growth hormone deficiency secondary to known intracranial pathology: 6 craniopharyngiomas, 1 pineal tumour, 1 neurofibroma, and 1 eosinophilic granuloma. The present ages of these patients vary from 7 to 22 years and in the Fig. the distribution of their years of birth are

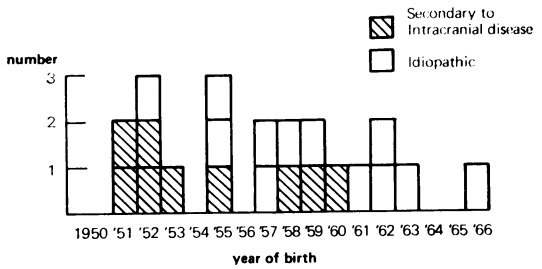

FIG.—*Year of birth of all patients with growth hormone deficiency.*

indicated. Secondary growth hormone deficiency is likely to present at an older age than idiopathic, and this is supported by the greater number of such patients in the earlier years.

It is probable that the majority of severely dwarfed children with growth hormone deficiency born between 1951 and 1962 will have presented. Older patients may not have been referred as treatment was not available when they were of the appropriate age, and those born later—especially those with intracranial pathology—may not yet have developed symptoms. During these 12 years 19 growth hormone-deficient patients were born, 10 with idiopathic deficiency and 9 with intracranial pathology. As the annual number of births in the Newcastle region is about 48,000 (*Registrar General*, 1970) these figures suggest that the annual incidence of growth hormone deficiency is 1 in 30,000 births, approximately half the patients having idiopathic growth hormone deficiency.

Community studies. It is possible that there are children in the community with growth hormone deficiency who are not referred to hospital because either their growth failure is not severe or their parents and doctors do not realize that any treatment is available. The Newcastle Survey of Child Development (G. A. Neligan, personal communication, 1974) has given an opportunity for a study of a total population of short children in Newcastle upon Tyne. All the children who were born in 1960 and whose heights were under the third centile at about 10 years and all the children born in 1961 and 1962 whose heights were more than 3 SDs below the mean at the same age were examined and their growth hormone levels measured after an exercise

stimulation test (Lacey and Parkin, 1974a, b). This meant that all the very short children from a population of about 8000 10-year-old children were examined. No clear case of organic growth hormone deficiency was discovered, there being good evidence of severe deprivation as the cause of the growth failure in the 3 children whose growth hormone levels were less than 10 μIU/ml. There was one patient among the children born in 1960 who possibly was an example of partial growth hormone deficiency. As her growth failure was not marked, it is unlikely that her parents will wish her to be given a trial of treatment.

Although the number of children screened in this study was not large enough to enable the incidence of growth hormone deficiency to be confirmed, it does indicate that the suggested incidence is not a gross underestimate.

Conclusion

Growth hormone deficiency is a very uncommon cause of short stature. Evidence is presented that indicates that when patients with low serum growth hormone levels associated with maternal deprivation are excluded, the approximate incidence of growth hormone deficiency is only 1 in every 30,000 births, about half of the patients having idiopathic deficiency and half having deficiency secondary to intracranial disease. If this is so only about 30 new patients who should benefit from growth hormone treatment may be expected to be diagnosed each year in England and Wales.

Summary

Evidence from the Newcastle upon Tyne region suggests that the incidence of organic growth hormone deficiency is about 1 in 30,000 births.

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Cor pulmonale in the Pierre Robin syndrome

Upper airway obstruction has only recently been recognized as a cause of cor pulmonale in childhood. Tonsillar and adenoidal hypertrophy are the most common predisposing factors (Menashe, Farrehi, and Miller, 1965; Luke *et al.*, 1966; Ainger, 1968), but laryngotracheomalacia (Cox *et al.*, 1965) and Crouzon's disease (Don and Siggers, 1971) have also been implicated. We describe a case of the Pierre Robin syndrome with severe upper airway obstruction who developed cor pulmonale at 5 weeks of age.

Case report

A male infant was born at home weighing 2·74 kg. He was transferred to hospital at 7 days with a history of feeding difficulty, stridor, and cyanotic episodes. On examination he had marked micrognathia and a large central palatal cleft. There were no other congenital abnormalities and in particular the heart sounds were normal; there were no cardiac murmurs and chest *x*-ray was normal.

He was nursed prone and fed by tube. He continued to have stridor and apnoeic spells, the frequency and severity of which were influenced by his head posture. At 5 weeks of age he had a sudden rise in weight accompanied by increasing respiratory difficulty and persistent cyanosis in air. On examination he had a precordial bulge and a forceful right ventricular parasternal thrust. The pulse rate was 180/minute. There was a third heart sound and summation gallop. A long systolic murmur was audible along the left sternal edge, coarse crepitations were heard over both lung fields, and the liver was palpable 3 cm beneath the right costal margin. Chest *x*-ray showed an enlarged heart, extensive soft lung shadowing consistent with pulmonary oedema, with some consolidation in the right upper lobe (Fig. 1a). ECG showed P pulmonale and changes of moderate biventricular hypertrophy. Repeated capillary blood samples taken from a warmed heel showed a persistent severe hypercapnia with P_{CO_2} 80–130 mmHg.

In an attempt to determine the posture in which respiratory obstruction was least, some studies of respiratory mechanics were carried out on the sleeping baby. Transthoracic pressure swings were recorded with an air-filled rubber balloon in the lower oesophagus; airflow and tidal volume were recorded by a pneumotachograph mounted in a face mask. Tidal volume, airflow, and oesophageal pressure swings were recorded while the baby was held in different positions. Pulmonary resistance was calculated by the pressure difference divided by the flow rate between midvolume points (Cook *et al.*, 1957). The results obtained (Fig. 2.) showed great variability in the airway resistance with only small changes in head posture. Resistance to airflow was least in the prone position with the face straight down (total pulmonary resistance 120 cm H_2O/l. per sec) and rose to infinity in the supine position. Oesophageal pressure swings varied from 10 cm H_2O (prone) to 40 cm H_2O (supine).

The baby was nursed prone with his neck partially flexed in the position which appeared to cause least airway resistance. His head was supported in a foam mattress in which a hole had been cut for his face. The