Discussion

There have been approximately 50 reported cases of Meckel syndrome since 1822 when Meckel first described the condition. Affected infants have multiple congenital defects including encephalocoele, microcephaly, microphthalmia, hare lip and/or cleft palate, small genitalia, polycystic kidneys, polydactyly, and a number of minor abnormalities (Hisia, Bratu, and Herbordt, 1971; Mecke and Passarge, 1971). For a positive diagnosis of the syndrome, Fried et al (1971) suggest that at least three of the major defects should be present. Although suggestive of a chromosomal aberration, particularly trisomy 13, the karyotype is normal, and the syndrome is thought to be due to an autosomal recessive gene (Mecke and Passarge, 1971). Affected infants are either stillborn or die shortly after birth. Both the second and third infants of this patient had multiple congenital anomalies which accord with the stigmata of Meckel syndrome. In view of the high recurrence rate in families (Fried et al, 1971; Hisa et al, 1971; Mecke and Passarge, 1971) and the fact that the first sib had microcephaly and an encephalocoele, it is possible that all three sibs had Meckel syndrome. Such a diagnosis is, of course, important for the future counselling of the patient.

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References


A case of hyalinosis cutis et mucosae (lipoid proteinosis of Urbach and Wiethoe) with common ancestors in four remote generations

Summary. We report a case of hyalinosis cutis et mucosae, a rare disorder of hyalin deposition in skin and mucous membranes, in a 27-year-old male, whose coefficient of inbreeding was 0.0106 due to seven common ancestors, including an aunt of an early American president, in the eight preceding generations.

Hyalinosis cutis et mucosae (lipoproteinosis, lipoid proteinosis of Urbach and Wiethoe) is a rare, chronic disease characterized by widespread papules, nodules, and plaques composed of hyalinized material. It may extensively involve the skin and the mucous membranes of the gastrointestinal, respiratory, and genitourinary systems, but it may occur as well in other organ systems, for instance, the central nervous system. The skin over the face, neck, and hands is frequently involved, although any area may be affected. The margins of the eyelids may present a distinct picture with papules distorting the lashes. There is predilection for lesions to occur on the mucosae of the oral cavity and upper respiratory tract. Hoarseness, which may present at birth, is a common sign produced by infiltration of the vocal cords. Microscopically the lesions show hyalinosis, that is, thickening of the capillary walls with deposition of hyalin beneath the basement membrane and in the dermis.

Hyalinosis cutis et mucosae is presumably monogenically determined as autosomal recessive, though a genetic analysis has not been published. The purpose of this report is to describe a case of the disorder in a 27-year-old male, the only child of his consanguineous parents, whose ancestry was traced and found to include seven common ancestors, including an aunt of an early American president, in four of the preceding eight generations.

Case report

The propositus (B.D.C. 0040-01-0571) was born when his mother was 42 and his father 48 years old, the result of their only pregnancy. During the gestation the mother required surgery at six months for a uterine
tumour, and the patient was born after 7 months with a birth weight of 1760 g. There was early difficulty both with feeding and hoarseness. He subsequently continued to have problems with his throat.

The diagnosis was established at 5 years. The next year he required removal of laryngeal polyps and 10 years later needed surgery for repair of bilateral inguinal herniae. Papules around his eyes have been disfiguring although not discomforting. However, soreness of the tongue and throat has required treatment.

He progressed satisfactorily in school—even being known as 'Froggy' at times—and matriculated to college where he was initially normally active; however, because of his worsening appearance, he gradually dropped out of social activities. He graduated in electrical engineering but has had trouble finding suitable employment, presumably because of his disfigurement and hoarseness. More recently he has developed a convulsive disorder.

His physical appearance was characterized by the presence of papular lesions around the eyes (Fig. 1) and by coarseness of the skin over the face and forehead with ridging and yellowish discoloration. We noted pitting and scarring of the face and forehead with small papular lesions in the area of his ears. There was scarring around the mouth and loss of papillae over the tongue (Fig. 2). We saw scarring and ridging in the posterior pharynx, and he was hoarse. Further, the texture of the skin of his abdomen suggested involvement. The skin over his elbows (Fig. 3) and knees showed hypertrophic papular lesions. There were verrucous changes over his palms, the dorsal aspects of his fingers, and over his feet. Lesions resembling acne occurred over the buttocks, and there was some nodular coarseness of the skin in the upper gluteal areas.

**Biopsy of the skin.** Thick homogeneous eosinophilic bands of hyalinized material surrounded the vessels and sweat glands with focal changes more evident in the lower dermis contrary to the more diffuse changes in the upper dermis.

**Clinical pathological studies.** Results of the study of serum showed: total lipids of 4.35 g/l (normal range for laboratory 4.0–7.0 g/l), fatty acids of 2.24 g/l (normal range 2.50–4.60 g/l), phospholipids of 1.80 g/l (normal 1.77–3.05 g/l), total cholesterol of 1.61 g/l (normal 1.50–2.80 g/l), and cholesterol esters of 74% (normal 70–75% of cholesterol). Results of routine studies of urine and blood were normal.

![Fig. 1.](image1)

Propositus at 25 years of age showing characteristic papules around the eyes (Fig. 1); scarring and loss of papillae over the tongue (Fig. 2); and hypertrophic papular lesions over the elbow (Fig. 3).

![Fig. 2.](image2)

![Fig. 3.](image3)

![Fig. 4. Pedigree.](image4)
The pedigree. The father of the patient had been particularly interested in genealogy and assembled the pedigree (Fig. 4). In four of the eight generations preceding the propositus there were seven common ancestors. From the nearest couple, who were great-grandparents of the father and great-great-grandparents of the mother, the parents were related to each other as second cousins, once removed. Proceeding to the more remote generations, the parents were related to each other from two common ancestors in generation III as third cousins, once removed, and from one common ancestor in generation II as fourth cousins, once removed. Finally, from two common ancestors in generation I their relationship was between that of fourth cousins, once removed, and fifth cousins as a result of the several different paths. Altogether, the coefficient of inbreeding, $F$, was 0.0106 for the propositus, which meant that his parents were related as more than second cousins, once removed ($F = 0.0078$) but less than full second cousins ($F = 0.0156$).

The feminine ancestor in generation I was an aunt of the third President of the United States, Thomas Jefferson; she was the sister of his father. We are unaware that this disease has ever been reported among his descendants.

Discussion

Hyalinosis cutis et mucosae is probably determined by a single gene transmitted as autosomal recessive (McKusick, 1971), though formal genetic analysis of a reasonable number of cases has not been published presumably because of the rarity of the disorder. In South Africa, Heyl (1970) has traced the disorder through generations spanning 300 years and found it to be autosomal recessive (Heyl, 1963). As a matter of fact, the disorder has been reported from South Africa more commonly than from anywhere else (Gordon, Gordon, and Botha, 1969). The mode of inheritance has seemed apparent from the lack of direct transmission, the frequency of affected sibs, and the commonness of parental consanguinity. There is as yet no evidence of genetic heterogeneity in spite of the report by Rosenthal and Duke (1967) of direct lineal transmission in two generations. In the family they reported, the parents, one of whom was affected, were related as full second cousins, and the a priori probability of the other being a carrier was 1/6 or 0.0625. That four of their five progeny were affected was somewhat unexpected, given that among five child families, only 0.015 would be expected to have precisely four affected on the hypothesis of an autosomal recessive gene. These four affected progeny had a total of 10 children, not one of whom was affected, an event expected as infrequently as 0.001 on a dominant gene hypothesis ($H$)10.

The parents of our patient were consanguineous which adds to the evidence for autosomal recessive determination of the disorder. That they were related as somewhat more than second cousins, once removed, but less than full second cousins was largely determined by the two common ancestors from whom they were descended as second cousins, once removed. The occurrence of several more remote common ancestors, albeit interesting in the construction of the pedigree, contributed just over one-fourth to the total coefficient of inbreeding.

The disfigurement and at least the laryngeal disability of our patient have created a social problem for him. This suggests the likelihood of selection against the gene in others who are perhaps similarly affected. Knowledge of the inheritance of the disorder affecting their son played no part in the decision of his parents not to bear other children, because the exact diagnosis was not made until the mother was menopausal and even then its heritability was not recognized.

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References


Neonatal testicular torsion in two brothers

Summary. Two brothers presenting neonatal testicular torsion are reported. The findings suggest an autosomal or X-linked recessive pattern of inheritance for the anatomical underlying anomaly.