LETTERS TO THE EDITOR

Osteoglophonic dysplasia

We read with interest the manuscript 'Osteoglophonic dysplasia', by Professor Peter Beighton (*J Med Genet* 1989;26:572–6). However, we would like to voice an objection to the spelling of the name of this disorder. Professor Jürgen Spranger suggested the term 'osteoglophonic dwarfism' on the basis of its radiographical findings.[1] The metaphyses appear to be 'hollowed out', so the term 'osteoglophonic' for 'hollowed bone' was proposed.

The Greek noun γλυφισ (genitive γλυφιδοσ) refers to the notch of an arrow (by which it is seated on the bowstring) and, by extension, to the arrow itself. The related verb γλυφω, γλυφειυ means "to hollow out, engrave, carve", and, by extension, "to write" (on a tablet). The Greek root persists in English as the suffix "-glyph", in "hieroglyph" or "petroglyph". The same root appears in many western European languages as a word meaning "to cut" or "to cleave", for example, in cleft palate. The Greek letter upsilon should be translated into English only as y or u. There is no reasonable English equivalent which uses the letter o for the Greek upsilon.

Therefore, we feel that this condition should be named correctly either 'osteoglyphic' or 'osteoglyphidic' dysplasia.

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1 Beighton P, Cremin BJ, Kozlowski K. Osteoglophonic dwarfism. *Pediatr Radiol* 1980;10:46–50.

Choanal atresia as a feature of ectrodactyly-ectodermal dysplasia-clefting (EEC) syndrome: a further case

Christodoulou *et al*[1] reported a family in which the proband had choanal atresia associated with the EEC (ectrodactyly-ectodermal dysplasia-clefting) syndrome. We wish to report another child with this syndrome, and choanal atresia, and confirm this feature to be associated with the EEC syndrome.

The proband presented with bilateral cleft of the lip and palate, preaxial polydactyly of the left foot, left hydronephrosis, right dysplastic and non-functioning kidney, and web penis. His mother has bilateral cleft of the lip and palate with no nail, hand, foot, hair, or tear duct abnormalities. However, the sib has classical features of EEC syndrome, including choanal atresia. In addition to very fair, brittle hair, she has bilateral absence of the tear ducts, facial dysmorphism consisting of underdeveloped philtrum, flat nasal bridge, and lateral placement of the inner canthi, and, in addition, syndactyly of fingers 3 and 4 on both hands. She has vesicoureteric reflux.

The diagnosis of the EEC syndrome in the proband and mother would have been difficult without the affected sib. This family also indicates the extreme variability and the renal tract anomalies seen in this syndrome.[2]

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1 Christodoulou J, McDougall PN, Sheffield LS. Choanal atresia as a feature of ectrodactyly-ectodermal dysplasia-clefting (EEC) syndrome. *J Med Genet* 1989;26:586–9.
2 Rollnick BR, Hoo JJ. Genitourinary anomalies are a component manifestation in the ectodermal dysplasia, ectrodactyly, cleft lip/palate. (EEC) syndrome. *Am J Med Genet* 1988;29: 131–6.

Paraplegia and arthrogryposis multiplex of the lower extremities after intrauterine exposure to ergotamine

In a recent issue of this Journal, Hughes and Goldstein[1] reported on a microcephalic girl with paraplegia, joint ankylosis, and anaesthesia of the lower limbs, suggesting medullar injury; lissencephaly and brain atrophy were also present. She was born after intrauterine exposure during the first four months of gestation to several vasoactive drugs: propranolol (80 mg/day) and 'cafergot' suppositories (one to four/week).

We recently observed a child with arthrogryposis congenita and paraplegia, whose mother took ergotamine in the fourth month of pregnancy. Our proband, a girl, was born at 32 weeks of a dizygotic twin pregnancy, obtained through in vitro fertilisation. Her brother weighed 2300 g and was normal. Her weight was 1720 g (50th centile) and OFC was 31 cm. Arthrogryposis multiplex of the lower limbs with sensorimotor nerve defect was present. The symptoms were very similar to the neurological status of a spina bifida aperta (or any other spinal cord trauma involving segments L1 to S1): bilateral equinovarus deformity of the ankles, bilateral fixation of the knees at right angles, and bilateral luxation of the hips, which were fixed in abduction-internal rotation. Moreover, perpartal fractures of both femora were present. There was both faecal and urinary incontinence and anal eversion. The thighs and buttocks were hypoplastic. There was some spontaneous movement at the ankle joints, as well as hip flexion, and some sensitivity remained in the plantar area and around the hip. The upper limbs were not involved. The face was normal.

Subsequent psychomotor development was normal, and partial motor and sensory recovery was observed. Transfontanellar ultrasonography and EEG were normal. Spine *x* ray, CT scan, and NMR imaging of the lower medulla oblongata were normal and excluded extrinsic compression or vertebral malformation. Electromyography showed a denervation pattern of fibrillations with some bursts of voluntary contraction in the quadriceps muscles. Prenatal cord trauma seemed the most probable aetiology, considering the muscle atrophy and ankylosis.

The parents were normal, nonconsanguineous Caucasians and there was no relevant family history. However, at 4½ months of gestation, the mother, who suffered from migraine, took one suppository of Cafergot® (Sandoz, composition: ergotamine 2 mg, caffeine 100 mg, belladonna alkaloid 0.25 mg, butalbytal 100 mg). She suffered from severe side effects including intractable nausea, vertigo, and dizziness, which confined her to bed for three days. The rest of the pregnancy was uneventful. Neither hydramnios nor oligohydramnios was recorded, nor a decrease in fetal movements.

The vascular effect of therapeutic or toxic doses of ergot alkaloid has been widely documented in man. Individual sensitivity to therapeutic doses of

ergotamine is variable and severe vaso-occlusion has been reported with therapeutic doses.[2] However, to our knowledge, paraplegia owing to occlusion of the lower medullary artery of Adamkiewicz does not seem to have been reported.

It has long been known that ergotamine crosses the placental barrier in small amounts.[2] David[3] described four of 24 patients with Poland's anomaly, where the mother attempted abortion with ergot derivatives and hypothesised that a defect of vascularisation in the limb bud induced by ergot could be responsible for the malformation.

We suggest that a single dose of ergotamine and caffeine administered at 4½ months could be associated, through placental transfer, with a vascular spasm of a medullary artery severe enough to induce spinal cord ischaemia and neuronal loss. Our observation, as well as the case reported by Hughes and Goldstein,[1] at least raises the possibility that ergotamine induced birth defects of vascular origin can occur.

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1 Hughes HE, Goldstein DA. Birth defects following maternal exposure to ergotamine, beta blockers, and caffeine. *J Med Genet* 1988;25:396–9.
2 Griffith RW, Grauwiller J, Model CH, Leist KH, Matter B. Toxicologic considerations. In: Berde B, Schild HO, eds. *Ergot alkaloid and related compounds*. Berlin: Springer-Verlag, 1978:805–51.
3 David TJ. Nature and etiology of Poland anomaly. *N Engl J Med* 1972;287: 487–9.

BOOK REVIEWS

HLA in Narcolepsy. Ed Y Honda, T Juji. (Pp 208; DM 156.) Heidelberg: Springer-Verlag. 1988.

This is a collection of articles about a condition characterised by the improbable combination of narcolepsy (falling asleep at inappropriate times), cataplexy (sudden loss of bilateral skeletal muscle tone triggered by emotion), hypnagogic hallucinations (vivid dreams usually of a threatening nature), associated with sleep paralysis (when the patient feels his whole body to be paralysed at the stage between arousal and sleep). This syndrome was first described as long ago as 1672 by Thomas Willis and many subsequent reports suggested its reality. The recent findings that all authenticated narcoleptic patients are HLA–DR2 positive provides proof of its organic and genetic basis.

The discovery followed the now familiar serendipitous pattern of HLA and disease associations. In an extensive study involving many genetic markers carried out by Akio Asaka, Yutaka Honda, and Takeo Juji in Tokyo the only significant associations were Bw35 (positive) and Bw52 (negative) in 58 narcoleptic patients. Much later studies of HLA–DR antigens showed the unexpectedly strong association with DR2 which has been subsequently confirmed in many parts of the world.

This is a well presented and interesting book with contributions from neurologists, HLA specialists, and others, covering most aspects of this disorder and its relationship with the HLA system. Although rather specialised it is only a slim volume and provides a fascinating insight into a whole new field of genetic and molecular studies in brain function and in behaviour.

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Genes and Signal Transduction in Multistage Carcinogenesis. Ed Nancy H Colburn. (Pp 480; $150.00.) New York, Basle: Marcel Dekker. 1989.

The title of this book is immediately attractive to anyone involved in the field of multistage carcinogenesis. For many years there has been a need for a book that provides a relatively up to date overview of the specialised animal model systems that can be correlated with the role of tumour promoting agents and specific genes which confer susceptibility to neoplastic transformation in signal transduction. The book is subdivided into four parts. Parts I and II deal with genetic variants for responses to mitogens and tumour promoters and with cloned genes that influence susceptibility to neoplastic progression. There is an excellent chapter on the genetic determinants of susceptibility to mouse skin tumour promotion by DiGiovanni and an excellent chapter by Herschman and Brankow on the suppression and expression of the transformed phenotype in $C_3H10T½$ cells following two stage transformation. The chapter by Weber and Schawver on the role of the *src* gene in cellular transformation provides some interesting information on 3T3–TNR9 cells, which are resistant to the mitogenic effects of the tumour promoter TPA, and not only fail to be transformed by *src* but are growth inhibited in the presence of the *src* gene. The other interesting discovery is that v-*myc* facilitates v-*src* transformation in these cells. Thus, the data suggest common steps in signal transduction by v-*src* and TPA and imply a role for *myc* in the pathway. Dr Colburn's own chapter shows that the promotion insensitivity of her JB6 promotion resistant cell line is not the result of altered levels of PKC, but is more likely to result from changes in critical substrates phosphorylated by PKC. There are also some cautionary notes in the very detailed chapter on the complex regulation of gene expression by TPA by Denhardt *et al;* we are reminded that a correlation between PKC activation and a change in gene expression does not signify a causal relationship. Gene expression during multistage carcinogenesis is reported in detail in the following chapter by Bowden *et al.*

The chapters in part III on signal transduction are excellent overviews of a very complex field and integrate well with the chapters mentioned above. There is an excellent introduction to the field in a chapter by Parker *et al* and nice discussions about the transduction of the phorbol ester signal and the role of PKC in IL–2 production in the following chapter. I particularly enjoyed the chapter on the role of *raf* and *myc* oncogenes in signal transduction by Heidecker *et al,* as I think we have dwelt on the role of *ras* in these messenger systems for too long. Finally, in part IV, on stress associated signals and gene regulation, there are two valuable chapters on the *fos* gene and *fos* protein. There is also an excellent chapter by Karin on cis and trans