Waardenburg's syndrome

SIR,

The unusual case of a man with features similar to Waardenburg's syndrome, multiple anomalies, and osteosarcoma, described by Parry *et al.*¹ prompted this comment on the relationship the multiple anomalies might have to the loose 'Waardenburg's syndrome' heading.

A stricter specific nomenclature is possible, since genetic heterogeneity has been demonstrated. There are two biometric groups: type 1 (WS1) with dystopia canthorum, and type 2 (WS2) without it. A third phenotype, also without dystopia, but with unilateral ptosis, has also been identified.^{2,3}

The difficulty has always been identification of dystopia canthorum. When establishing the division into three types, a biometric tool was introduced.² Recently, a new index called W⁴ has allowed unequivocal differentiation of Waardenburg's syndrome with dystopia (WS1) from that without it (WS2) in more than 96% of cases; the remaining 4% are included in an intermediate biometric group with 'non-apparent dystopia' (NAD). Non-dystopic (80% of both normal and WS2) subjects have a W index of <1.87 , while only 6% of normal subjects have $2.07 > W \geq 1.98$; most WS2 subjects have $W < 1.87$ and none has $W \geq 1.98$.⁴

The W index for the patient described by Parry *et al.*¹ is 2.04. He is also at the boundary for blepharophimosis, as index P, another biometric tool, is 0.59 (if $P < 0.57$, blepharophimosis is present).⁴ Thus, this patient has WS1. This is an important conclusion, since it is probable that no WS2 subjects will be found with associated congenital malformations, but only those with WS1.

Confirmation that WS1 is associated (although at a moderate frequency) with visceral malformations⁵ seems sound. Absence of this association in WS2 patients makes it less probable that WS1 and WS2, both autosomal dominant phenotypes, result from allelic mutations. On the other hand, the rare cases

described by Klein⁶ and Wilbrandt and Ammann⁷ with severe multiple malformations would be good candidates for alleles at the *WS1* locus.

Orbital measurements are absolutely necessary for the ascertainment of genetic heterogeneity in Waardenburg's syndrome. Good differentiation should shed light on developmental problems, as well as genetic ones like linkage relationships.⁸ The simple but reliable formulae available allow the differentiation of each type. Measurements should always be taken and published, as in the case of Parry *et al.*¹ to avoid subjective analysis and to further knowledge.

A simple programme for a programmable pocket calculator to estimate suitable indices is available on request.

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