

This letter was shown to the authors, who reply as follows:

SIR,—We thank Professor Anderson for his pertinent reminder of the importance of morphological factors in congenital heart disease and their potential relevance to the treatment of patients with aortic stenosis. The reason that data on valve morphology were not included in our report is that we believe it is often difficult to be certain of leaflet morphology based solely on echocardiography in neonates with severe aortic stenosis. The poor correlation between echocardiographic predictions and observed morphology at the time of surgery was well described in the paper by Leung and Anderson.¹ In their study, echocardiographic examination of 20 infants with critical aortic stenosis identified 16 with bicuspid valves, four with tricuspid valves, and no unicuspid valves. This contrasts with the surgical findings in the same infants where six valves were described as unicuspid, 13 bicuspid, and 1 tricuspid.

In the patients we studied,² the aortic valve was considered to be bicuspid in six, tricuspid in five, and one may have had a unicuspid valve. Because few of these patients had visual inspection of the aortic valve (either surgically or at necropsy) we are unable to comment on the validity of the echocardiographic findings. There did not seem to be any correlation between echocardiographically determined valve morphology and outcome. The principal determinants of survival being left ventricular (rather than aortic valve) dimensions and presence and severity of associated lesions. The patient with the apparently unicuspid valve had an excellent response to balloon valvoplasty.

It does, however, seem logical to believe that aortic valve morphology may have an important influence on the degree of relief of valve obstruction obtained, on the propensity for early re-stenosis, and on the maintenance of longer term valve competence. Studies of the relation between valve morphology and the outcome of balloon dilatation might be of considerable interest. Precordial echocardiography may not be adequate for such cases, where transoesophageal echocardiography or intravascular ultrasound may be of additional value.

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Familial atrioventricular septal defect: possible genetic mechanism

SIR,—We read with interest the report of Kumar *et al* describing a family in which the mother and her two daughters by different fathers had atrioventricular septal defects not associated with trisomy 21.¹ They suggest that an autosomal dominant pattern of inheritance may be involved in this pedigree, although a multifactorial or cytoplasmic mechanism cannot be ruled out.

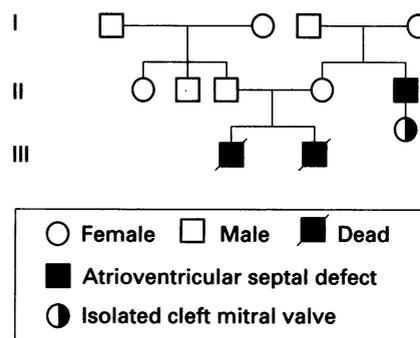
We recently described five families in which two or more members had isolated atrioventricular septal defect. Parent-to-son transmission of concordant cardiac defect was documented in four cases. The mother was affected in three cases and the father in one.²

Lately we found an additional example of atrioventricular septal defect in four members in two generations of the same family (figure). None of the family members showed phenotypic anomalies and all had a normal karyotype. They were examined by electrocardiography and echocardiography. A partial atrioventricular septal defect was diagnosed in one case (II 5) and a complete defect in two cases (III 1 and III 2). The daughter of a patient with atrioventricular septal defect had an isolated cleft of the mitral valve (III 3).

Anatomical differences between isolated mitral clefts and clefts associated with an atrioventricular septal defect have been described.³ The high frequency of isolated mitral cleft in families with atrioventricular septal defects,^{4,5} including our family, and its prevalence in patients with Down's syndrome (4/420 *v* 3/5200 in our experience), however, suggests that this malformation should be included in the spectrum of atrioventricular septal defects.

Monogenic autosomal dominant inheritance with incomplete penetrance could explain the atrioventricular septal defects in the families we studied and those reported by other workers. Normal parents of affected children could be obligate carriers of the gene involved in familial atrioventricular septal defects. The father-to-daughter transmission of cardiac malformation in two cases excludes cytoplasmic inheritance in these families. Moreover, atrioventricular septal defects in patients with and without Down's syndrome differ not only in terms of the prevalence of partial or complete forms^{6,7} but also in terms of the distribution of associated cardiac malformations.^{6,8} These anatomical differences and the absence of linkage in the molecular analysis of chromosome 21 in families with atrioventricular septal defect^{9,10} suggest that the gene or genes involved in the pathogenesis of atrioventricular septal defect in "normal" children are different from those in patients with Down's syndrome.

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Pedigree

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