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Familial recurrence of discrete membranous subaortic stenosis

We read with interest the article by Fatimi and colleagues¹ published in a recent issue of the *Journal*.

The authors report on 2 siblings affected by discrete membranous subaortic stenosis (DMSS), who were born to unaffected consanguineous parents. Literature reports of familial recurrence of DMSS were reviewed, and conclusions were that "review of the pedigrees and the information provided in the published reports does not reveal a clear inheritance pattern."

Nevertheless, we believe that Mendelian autosomal recessive inheritance may be considered as the main mechanism involved in the cause of concordant recurrence of DMSS in families on the basis of several observations. First, at least 8 families with recurrence of DMSS in siblings are reported in the literature,¹⁻⁵ including 2 sisters with DMSS born from unaffected consanguineous parents described by our group in 1993² (Figure 1, a). Second, parental consanguinity was observed in 4 families with recurrence of DMSS in siblings, including ours.^{1,2,4} Third, the recurrent cardiac defect is anatomically concordant in affected siblings from pedigrees with horizontal familial recurrence.¹⁻⁵

Obviously, genetic heterogeneity is implicated in the cause of DMSS, and the autosomal dominant inheritance with incomplete penetrance may be hypothesized in several instances.¹ In fact, parent-to-child transmission or segregation in uncle and nephew may be explained in this matter. In our 6-year (1993–1999) investigation of family history in patients affected by nonsyndromic DMSS, 3 additional pedigrees with familial recurrence of cardiac

defect have been detected (Figure 1, b-d). Cardiac defect was concordant in 1 family (Figure 1, b). In addition, a mother with DMSS had a child with aortic coarctation and valvar aortic stenosis (Figure 1, c), and a proband with DMSS had a cousin affected by tetralogy of Fallot (Figure 1, d). A multifactorial model of inheritance, suggesting that several chromosomal loci could interact together in association with environmental factors, may also be involved, particularly in sporadic cases and in families with recurrence of discordant cardiac defect.

Although DMSS is usually considered an "acquired" cardiac defect with delayed clinical presentation, the possibility of familial recurrence suggests a genetic substrate at least in some cases.

The genetic basis of DMSS is still unknown. In the future, molecular studies will provide an important aid in the interpretation of familial recurrence of DMSS. Genetic heterogeneity of DMSS probably includes the involvement of different genes. Similarly to that documented in some families segregating conotruncal heart defects, some genes may act accordingly to the autosomal recessive mechanism of inheritance,⁶ whereas others may follow the autosomal dominant model with incomplete penetrance.^{7,8}

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Figure 1. a-d, Four pedigrees with recurrent cardiac defect from our series of patients with DMSS. DMSS, Discrete membranous subaortic stenosis.

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Reply to the Editor:

We thank Piacentini and associates for their interest in our article¹ and for their expert opinion on the topic. We would like to focus on three things.

The authors have discussed three new pedigrees of discrete subaortic stenosis (DSS), only one of which actually has true familial recurrence of DSS. The other two have family members affected by other forms of congenital heart defects, which may or may not have the same genetic basis. Their discussion, however, reiterates our conclusions that no single inheritance pattern can be pinpointed by reviewing the currently available evidence. Genetic heterogeneity and incomplete penetrance could also be important players. We agree with the authors concerning the autosomal recessive inheritance, and we think that given the currently available evidence there is a greater probability of autosomal recessive inheritance being at play in the familial causation. At the same time, most families with multiple affected members do not have consanguineous marriages, and this argues against involvement of recessive alleles. Hence no conclusion can be reached.

Second, as seen in acquired cardiovascular diseases, there may be differences in the relative contributions of the involved genes toward causing the phenotype in the various ethnic groups. Therefore, the pooling and comparison of data from different population subgroups may actually be misleading. However, owing to the scarcity of familial DSS patients at any one center, we still recommend a multicenter approach to get enough sample size for efficient genetic screening.

Last, it is important to reinforce the fact that screening of family members of appar-

ently sporadic cases can lead to timely diagnosis and better follow-up of familial cases.

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Bovine jugular vein as aortic enlargement patch in the Norwood procedure

To the Editor:

We have read with interest the brief communication by Healy and colleagues,¹ in which they describe a new and innovative technique, never before published, concerning use of a bovine jugular vein as an augmentation patch in the Norwood procedure.

The original technique described by Norwood, Lang, and Hansen² involved the use of a homograft to enlarge the aorta. The lack of availability, its high cost, and the risk of infection induced some surgeons to use alternative patches. In fact, in 1999 Gargiulo and associates³ described aortic augmentation with a bovine pericardial patch.

We were very enthusiastic about the Healy report in the *Journal*, both for its contribution to the research toward new alternative materials with respect to homografts in the Norwood procedure and because this technique is similar to our recent surgical strategy.

In 23 Norwood cases, we have used a Contegra patch (Medtronic, Inc, St Paul, Minn) to enlarge the aorta. Technically, we remove the jugular vein with the valve in it and we open the Contegra patch to perform aortic enlargement. The operative technique is not more complex than the original technique with the homograft. Our results were very fulfilling and were similar to

these described in the literature with the classic Norwood operation. We prefer to use this conduit to reduce the risk of viral transmission and especially to reduce the risk of immunologic sensitization, as been described by Meyer and associates.⁴ Besides these benefits, the cost is lower.

We hope that our positive experience can bring a little support to the Healy experience and technique.

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Improved saphenous vein graft patency for coronary artery bypass grafting: "No-touch" harvesting or "dissection without touching"?

To the Editor:

A recent article in the *Journal* described the beneficial effect of penicillamine in a widely established porcine saphenous vein—carotid artery interposition model.¹ This, and previous porcine vein graft studies use a "no-touch" technique of preparing saphenous veins that was described 30 years ago by Gottlob.² This technique was developed using saphenous vein segments obtained from bypass operations or cadavers and canine femoral veins. The aim of this preparation of "dissection without touching" (the term "no-touch" seems to have crept into the literature) was to preserve the vein's endothelium by a rather unwieldy method in which "the venous