Characterization of the Cardiomyopathy in Infants of Diabetic Mothers

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SUMMARY A transient form of hypertrophic cardiomyopathy has been previously described in infants of diabetic mothers (IDMs). The purpose of this study was to determine the incidence, natural history and pathologic features of this cardiomyopathy in symptomatic and asymptomatic IDMs.

We studied 47 IDMs for evidence of cardiomyopathy. Among 24 symptomatic IDMs, five had marked septal hypertrophy with echocardiographic features suggesting left ventricular outflow obstruction and five had hypertrophy of the right ventricular free wall. With the exception of mild septal hypertrophy, these abnormalities resolved during the first 6 months of life, and echocardiograms in the first-degree family members were normal. Of 23 asymptomatic IDMs, three had septal hypertrophy and two had right ventricular free wall hypertrophy; none of the asymptomatic IDMs had evidence of outflow obstruction.

One symptomatic IDM died, and autopsy revealed a hypertrophic septum that distorted both ventricular cavities. Microscopic examination revealed hypertrophic fibers and occasional areas of cellular disarray in the septum.

Despite the clinical and pathologic similarities of the cardiomyopathy in IDMs to the hypertrophic cardiomyopathies in older children and adults, its transient and nonfamilial nature suggest that it is a separate disease. We speculate that it is a manifestation of the generalized organomegaly in IDMs.

SINCE THE MID-1940s, clinicians have recognized cardiac enlargement in many infants of diabetic mothers (IDMs). Early reports did not establish the cause of the cardiomegaly, but did note that it usually resolved within the first 6 months of life.1,2 Preliminary studies3-6 have shown that IDMs may have a transient form of hypertrophic cardiomyopathy. We have further characterized this disorder by studying its incidence in symptomatic and asymptomatic IDMs. We have also studied the gross and histologic features of this cardiomyopathy in an infant who died at 2 weeks of age.

Materials and Methods

Three groups of newborn infants form the basis of this report — two groups of IDMs and a control group of normal newborns. Echocardiograms were performed on all infants. ECGs, chest roentgenograms, follow-up echocardiograms and family studies were obtained in selected patients.

Group 1 — Symptomatic IDMs

This group consisted of 26 IDMs admitted to the neonatal intensive or intermediate care nursery of the Texas Children's Hospital because of one or more of the complications of maternal diabetes. Two infants had congenital heart disease (one case each of tetralogy of Fallot and aortic atresia) and were excluded from analysis. Respiratory distress was the most common symptom and was present in 20 patients, 12 of whom required intubation and assisted ventilation. Hypocalcemia was present in 12 patients and hypoglycemia in 11. The severity of the maternal diabetes was scored by a modification of the White classification.7 In this system, gestational or "chemical" diabetes is considered class A, long-standing, insulin-dependent diabetes with vascular disease and nephritis is class F, and diabetes of intermediate severity is considered classes B, C or D, depending on duration and need for insulin. Among the patients in this group, the maternal diabetes was class A in six, B in six, C in 11 and D in one. Each patient in this group had an ECG and 20 had at least one chest roentgenogram.

Group 2 — Asymptomatic IDMs

The second group consisted of 23 asymptomatic IDMs. These patients were studied prospectively, in cooperation with the obstetrical service. In the 6-month period July 1-December 31, 1977, 30 IDMs were born at St. Luke's Episcopal Hospital and the Texas Women's Hospital. The parents of each infant were asked to participate in the study and 25 agreed to do so. In these families, the details of the pregnancy were recorded, the infant was examined for the presence of heart disease, and an echocardiogram was performed on the infant, just before or within 1 week after hospital discharge. Satisfactory echocardiograms were obtained in 23 of the infants.

The severity of the maternal diabetes was as follows: class A in 14, B in six, C in one and D in two. None of these infants had illness related to maternal diabetes and none received therapy other than prophylactic glucose infusion to prevent hypoglycemia. Gestational age was greater than 36 weeks in all infants and mean birth weight (3514 ± 115 g) was similar to that of the control group.
Group 3 — Controls

This group consisted of 20 normal newborns of healthy mothers. These infants had no heart disease as judged by history and physical examination. Echocardiograms were performed during the first week of life. Informed consent was obtained from the parents and the primary physician before study.

Echocardiograms

The echocardiograms were obtained with Hoffrel ultrasonoscopes, models 101 and 201, coupled to Honeywell model 1856 strip-chart recorders. Transducers of 3.5 or 5.0 MHz were used. In each patient, the following measurements were made: septal thickness, right ventricular (RV) wall thickness, RV cavity diameter, left ventricular (LV) posterior wall thickness, LV end-diastolic diameter (EDD) and total cardiac diameter. These measurements were made at the onset of the QRS complex of lead II of the ECG, from recordings in which both the anterior and posterior leaflets of the mitral valve were visualized. The cardiac diameter was the distance from the anterior edge of the RV free wall to the LV pericardium. LV end-systolic diameter (ESD) was measured at the point of closest approximation of the septum and posterior wall in late systole. Additionally, LV outflow tract diameter was measured on an aorta-to-left ventricle sweep. The outflow tract diameter was considered to be the distance between the anterior mitral leaflet and the septum in the region immediately below the aortic valve, measured at end-systole. All measurements were rounded off to the nearest millimeter. The percentage shortening of the LV minor-axis diameter (\%ΔLVD, or “shortening fraction”) was calculated as follows: (EDD - ESD)/EDD × 100.

Echocardiographic Criteria for Hypertrophy

In neonates, the RV anterior wall and LV posterior wall were considered hypertrophic if their thickness was 5 mm or greater; the septum was considered hypertrophic if it was 6 mm or greater. Patients with a ratio of septal-to-LV posterior wall thickness of 1.3 or greater were diagnosed as having asymmetric septal hypertrophy. These criteria are based on the data from the normal newborns in the present study (table 1), as well as on data from the normal newborns studied by Solinger et al.,8 Hagan et al.,9 and Rogé et al.10 In the follow-up studies of the symptomatic

| Table 1. Echocardiograms, Electrocardiograms and Chest Roentgenograms in Normal Newborns (Group 3) |
|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|-----------------|
| Pt   | RVAW | RV | IVS | LVPW | IVS/LVPW | EDD | %Δ | LVOT | TCD |
| 1    | 3     | 8  | 4   | 4    | 1.0     | 16  | 25 | 7    | 32  |
| 2    | 3     | 8  | 4   | 3    | 1.3     | 18  | 33 | 8    | 35  |
| 3    | 2     | 9  | 4   | 3    | 1.3     | 17  | 29 | 7    | 34  |
| 4    | 3     | 9  | 4   | 3    | 1.3     | 18  | 33 | 7    | 33  |
| 5    | 4     | 10 | 4   | 4    | 1.0     | 17  | 29 | 8    | 38  |
| 6    | 3     | 9  | 4   | 3    | 1.3     | 16  | 38 | 7    | 32  |
| 7    | 4     | 10 | 4   | 4    | 1.0     | 17  | 35 | 6    | 34  |
| 8    | 3     | 9  | 4   | 3    | 1.3     | 11  | 36 | 6    | 27  |
| 9    | —     | —  | 4   | 3    | 1.3     | 16  | 31 | 6    | 34  |
| 10   | 4     | 10 | 4   | 3    | 1.3     | 16  | 31 | 7    | 34  |
| 11   | —     | —  | 4   | 4    | 1.0     | 15  | 33 | 7    | 32  |
| 12   | 3     | 8  | 4   | 3    | 1.3     | 16  | 38 | 6    | 31  |
| 13   | 4     | 8  | 4   | 3    | 1.3     | 17  | 35 | 7    | 35  |
| 14   | 3     | 8  | 4   | 4    | 1.0     | 16  | 38 | 6    | 31  |
| 15   | 3     | 10 | 4   | 4    | 1.0     | 18  | 33 | 6    | 38  |
| 16   | 3     | 9  | 4   | 3    | 1.3     | 17  | 35 | 7    | 33  |
| 17   | 3     | 10 | 4   | 3    | 1.3     | 18  | 33 | 6    | 34  |
| 18   | —     | —  | 4   | 4    | 1.0     | 16  | 38 | 8    | 36  |
| 19   | 4     | 10 | 5   | 4    | 1.2     | 18  | 33 | 6    | 32  |
| 20   | —     | —  | 4   | 3    | 1.3     | 17  | 35 | 7    | 34  |
| Mean | 3.2   | 9.1| 4.0 | 3.4  | 1.2     | 16.5| 33.6| 6.8  | 33.4|
| SD   | 0.6   | 0.8| 0.2 | 0.5  | 0.1     | 1.6 | 3.4 | 0.7  | 2.5  |

All measurements are in millimeters.
Abbreviations: RVAW = right ventricular anterior wall; RV = right ventricular; IVS = interventricular septum; LVPW = left ventricular posterior wall; EDD = left ventricular end-diastolic diameter; %Δ = percent change in left ventricular diameter; LVOT = left ventricular outflow tract diameter; TCD = total cardiac diameter.
IDMs echocardiographic data were compared with normal values for older children studied in our laboratory.\textsuperscript{11}

Statistical Methods

The echocardiographic measurements and birth weights of the three groups were compared by analysis of variance. The null hypothesis that the three groups did not differ was rejected if the probability of intergroup difference occurring by chance was less than 0.05.

Results

Symptomatic IDMs

In symptomatic IDMs, the ventricular walls were hypertrophied. The mean thicknesses of the RV anterior wall, the septum and the LV posterior wall were greater than those in the normal infants (table 1, fig. 1). The RV wall was hypertrophied in four patients, the septum in 11 and the LV posterior wall in 10. Although the hypertrophy was generalized, it was most notable in the ventricular septum. In five patients, septal thickness approached or exceeded twice that of normal newborns (table 1). Asymmetric septal hypertrophy was present in 11 of the 24 symptomatic IDMs. The mean RV cavity diameter was normal and the LV diameter was slightly smaller than normal (15.5 ± 0.30 mm [SEM] vs 16.5 ± 0.35 mm, \( p < 0.05 \)). The \%ΔLVD and the total cardiac diameter were normal in the symptomatic IDMs (table 2).

Five of the symptomatic IDMs had echocardiographic findings suggestive of LV outflow obstruction. Each of these patients had systolic anterior motion of the mitral valve, which brought it into apposition with the septum (fig. 2). In addition, each of these patients had midsystolic closure or fluttering of the aortic valve leaflets (fig. 3), and an LV outflow tract diameter of less than 5 mm (normal mean 6.8 mm, range 6–8 mm). In one infant with echocardiographic features of outflow obstruction, cardiac catheterization and angiography revealed a gradient of 30 mm Hg across the LV outflow tract and marked septal hypertrophy.\textsuperscript{3}

There was no apparent relationship between the severity or duration of the maternal diabetes and echocardiographic findings. The White classification of severity of diabetes in the mothers of the five most severely affected infants was A in three, B in one and C in one. Among the infants born to the 13 mothers with class C or D diabetes, one had features of outflow obstruction, two had septal hypertrophy, two had septal and RV wall hypertrophy and eight had normal echocardiograms.

The electrocardiogram was normal in 12 of the symptomatic IDMs and showed right ventricular hypertrophy (RVH) in seven and biventricular hypertrophy (BVH) in five. The ECG was abnormal in each of the five symptomatic IDMs with echocardiographic evidence of LV outflow obstruction and showed RVH in three and BVH in two. In general, however, there was no consistent relationship between the electrocardiographic evidence of ventricular hypertrophy and the echocardiographic findings (table 2).

Portable chest roentgenograms in the anteroposterior projection were obtained in 20 of the symptomatic IDMs. In eleven of these patients, the cardiac silhouette appeared enlarged and the cardiothoracic ratio was 0.65 or greater. The radiographic estimate of heart size was not directly related to the echocardiographic findings. Cardiomegaly by chest roentgenogram could not be explained consistently by increased ventricular chamber diameter, wall thickness, or total cardiac dimension (table 2).

Follow-up Studies

Serial echocardiograms were performed on the four symptomatic infants with the greatest degree of septal hypertrophy (table 3). Signs of outflow obstruction...
resolved by 3 months of age in each patient. Septal thickness became normal in two of these infants by 3 months of age (fig. 4); the other two have mild septal hypertrophy and septal/posterior wall ratios of 1.5 at 20 and 24 months of age. LV and RV wall thicknesses were normal in each infant by 6 months of age.

Family Studies

There was no history of congenital heart disease, cardiomyopathy or sudden unexplained death in the families of the five infants with evidence of LV outflow obstruction. Echocardiograms performed on 11 of the

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Mean 3.9* 8.8 6.6† 4.5† 1.4 15* 36.1 6.1 35.4

sd 0.8 2.0 2.8 0.8 0.5 2.7 8.3 1.4 4.1

*p < 0.05 vs normal.
†p < 0.01 vs normal.

Abbreviations: LVOTO = left ventricular outflow tract obstruction; X-ray = cardiomegaly by chest roentgenogram; + = present; N = normal; RVH = right ventricular hypertrophy; BVH = biventricular hypertrophy; for other abbreviations see table 1.
14 first-degree relatives of these infants were normal. In particular, there were no cases of asymmetric septal hypertrophy.

**Asymptomatic IDMs**

Mild ventricular wall hypertrophy was present in the asymptomatic IDMs. Mean septal thickness and posterior wall thickness were greater than normal (table 4). In eight of these patients, septal thickness was 5 mm and in three it was 6 mm (fig. 5). Three patients had asymmetric septal hypertrophy and two patients had RV free wall hypertrophy. The RV diameter, %ΔLVD, LV outflow tract diameter and total cardiac diameter were normal. The LVEDD was slightly smaller than normal (15.5 ± 0.3 mm vs 16.5 ± 0.3 mm, p < 0.05). None of the asymptomatic IDMs had echocardiographic features of LV outflow obstruction.

**Postmortem Examination**

One symptomatic IDM (patient 2; table 2) died of bacterial sepsis at 2 weeks of age. She had been born at term to a 38-year-old class B diabetic mother whose diabetes was controlled with oral hypoglycemic drugs. The ECG showed BVH and the chest roentgenogram showed moderate cardiomegaly and increased pulmonary venous markings. An echocardiogram revealed marked hypertrophy of the septum. The thickness of the septum was over 15 mm, that of the posterior wall 6 mm. The LV cavity was small (EDD 12 mm), and there was systolic anterior motion of the mitral valve and midsystolic closure of the aortic valve.

At autopsy, the enlarged heart had a prominent left ventricle. The great arteries and the atrioventricular and semilunar valves were normally oriented. The heart was sectioned in a frontal plane, revealing hypertrophy of the LV and RV walls and the septum. The hypertrophic septum distorted both ventricles (fig. 6). The septal thickness was 15 mm and the posterobasal LV free wall thickness (excluding trabeculae) was 8 mm, a ratio of 1.9. The RV free wall thickness was 7 mm. The LV endocardium was normal, as was the anterior mitral leaflet.

Microscopically, the fibers of both ventricles, but particularly of the left, were hypertrophic. Subendocardial areas of necrosis, accompanied by interstitial edema and a mononuclear inflammatory infiltrate, were present in the left ventricle. Scattered areas of the ventricular septum, but not the free wall of the right or left ventricle, contained irregularly shaped and oriented muscle fibers (fig. 7). These fibers

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**TABLE 3.** Serial Echocardiograms In Symptomatic Infants of Diabetic Mothers (Group 1)

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<th>Age</th>
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*Value greater than normal based on body weight.3-11 Abbreviations: SAM = systolic anterior motion of the mitral valve; MSC = midsystolic closure of the aortic valve; for other abbreviations see table 1.
FIGURE 4. A) Echocardiogram showing marked septal hypertrophy in a 1-day-old, symptomatic (respiratory distress) infant of a diabetic mother. On some beats, systolic anterior motion of the mitral valve brings it against the septum. B) Echocardiogram of the same patient at 3 years of age. Septal thickness is normal for age (7 mm), as is the thickness of the posterior wall and the motion of the mitral valve. RV = right ventricle; IVS = interventricular septum; LVPW = left ventricular posterior wall; MV = mitral valve.

Discussion

The results of this study indicate that some IDMs have a unique, apparently transient, form of cardiomyopathy. The ventricular walls are thick, ventricular internal dimensions are normal or decreased and LV systolic function is normal by echocardiography. Although others have reported evidence of a dilated or congestive cardiomyopathy in some IDMs, we could not find it in any of the 47 IDMs we studied.

Although the chest roentgenogram and the ECG were frequently abnormal in the symptomatic IDM, they appear to be less specific than the echocardiogram in delineating the specific abnormality in these patients. The lack of correlation between the radiographic and echographic findings is not entirely unexpected; the techniques image the heart in different planes and the cardiac silhouette on the radiograph may include the left atrial appendage, main pulmonary artery and thymus, structures not included by conventional echocardiograms.

The echocardiographic, hemodynamic and histologic features of this condition are similar to those of familial hypertrophic cardiomyopathy. We have
Table 4. Echocardiograms, Electrocardiograms and Chest Roentgenograms in Asymptomatic Infants of Diabetic Mothers (Group 2)

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Mean 3.6 8.3 4.6† 4.2† 1.09* 15.5* 32 6.52 34
sd 0.7 1.4 0.8 0.6 0.16 1.4 5.4 0.59 2.6

All measurements are in millimeters.
* p < 0.05 vs normal.
† p < 0.01 vs normal.

Abbreviations: see table 1.

been unable to identify cardiomyopathy in the first-degree relatives of the five infants with echocardiographic evidence of LV outflow obstruction or in the family of another IDM studied by cardiac catheterization. However, we studied relatively few family members per proband. Although familial hypertrophic cardiomyopathy is considered to be an autosomal dominant condition with a high degree of penetrance,18 our failure to find family members with asymmetric septal hypertrophy does not prove that

Figure 5. Echocardiogram from an asymptomatic infant of a diabetic mother. Septal thickness (IVS) is slightly increased (6 mm); left ventricular posterior wall thickness (LVPW), right ventricular (RV) and left ventricular (LV) cavity dimensions and mitral valve (MV) motion are normal.
the cardiomyopathy of IDMs is a different disease entity.

The tendency for the echocardiographic abnormalities to disappear is also unlike the natural history of other forms of hypertrophic cardiomyopathy. Although children with familial hypertrophic cardiomyopathy may be asymptomatic, clinical deterioration and sudden death are not uncommon; to our knowledge, spontaneous resolution of this condition has not been reported. Whether the cardiomyopathy of IDMs entirely resolves may be questioned. Although the features of LV outflow obstruction disappeared in the first 6 months of life, two patients have mild degrees of asymmetric septal hypertrophy in the second year of life.

Autopsy studies have confirmed the clinical impression of cardiac hypertrophy in IDMs. Early reports of myocardial glycogen deposition have not been substantiated. Using quantitative microscopic techniques, Naeye found an increase in the mass of both myocardial nuclei and sarcoplasm in the hearts of overweight IDMs. The histologic appearance of the myocardium in our patient is of particular interest in view of the echocardiographic, hemodynamic and gross cardiac similarities between the cardiomyopathy of IDMs and other forms of hypertrophic cardiomyopathy. Familial hypertrophic cardiomyopathy is characterized by asymmetric septal hypertrophy and a histologic pattern of myocardial fiber disorganization. Recent studies have shown that both of these findings may be less specific than previously thought; asymmetric septal hypertrophy has been demonstrated in a variety of conditions and in the normal fetus. Myocardial fiber disorientation has been found in the ventricles of infants with aortic and pulmonic atresia. The recent work of Maron and Roberts suggests that the extent of cellular disorganization, rather than its presence or absence, is the important histologic criterion for familial hypertrophic cardiomyopathy. Thus, although the pattern of cellular disarray present in our patient was qualitatively similar to that seen in familial hypertrophic cardiomyopathy, its limited distribution was more typical of other forms of heart disease.

The lack of asymmetric septal hypertrophy in family members, the tendency for the hypertrophy to decrease with time and the limited extent of the histologic abnormalities cause us to believe that the cardiomyopathy of IDMs has a different etiology than familial hypertrophic cardiomyopathy. The babies of diabetic mothers are typically large for gestational age and often have generalized organomegaly. Maternal hyperglycemia, with resultant fetal hyperglycemia, stimulates fetal islet cells and produces persistent fetal hyperinsulinemia, which may promote increased

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**Figure 6.** Frontal plane section of the heart of a symptomatic infant of a diabetic mother. The hypertrophic ventricular septum bulges into the outflow tract of the left ventricle. The free walls of both ventricles are also hypertrophied, although to a lesser degree. IVS = interventricular septum; RV = right ventricle; PW = left ventricular posterior wall; LA = left atrium.

**Figure 7.** Microscopic section from the interventricular septum of an infant of a diabetic mother. Note the irregularly shaped fibers with a distorted orientation, forming whorls and S-shaped bands (Gomori's trichrome stain; magnification × 160).
glycogenesis, lipogenesis and protein synthesis, with resultant obesity and macrosomia. Breitweser et al. described septal hypertrophy in a neonate with nesidioblastosis (ductoinsular cell proliferation) and hyperinsulinemia, further evidence that elevated insulin levels may be related to cardiac hypertrophy. We speculate that the cardiac hypertrophy of IDMs represents another manifestation of their generalized organomegaly.

The finding of more traditional forms of congenital heart disease (tetralogy of Fallot and aortic atresia) in two of 26 symptomatic IDMs is consistent with the increased incidence of heart disease in the children of diabetic mothers. Rowland et al. found the incidence of congenital heart disease in IDMs five times greater than that in the general population. Heart murmurs and cardiomegaly were present in nearly one-third of their “control” group of IDMs without congenital heart disease. Echocardiography was not performed, and some of these infants may have had the cardiomyopathy described in the present report.

The results of this study have several implications regarding the therapy of IDMs. First, it should not be assumed that the large cardiac shadow on chest roentgenogram represents a dilated, poorly contracting heart. We believe that therapy with digitalis or other positive inotropic agents is contraindicated unless depressed myocardial contractility can be proved. Second, although IDMs may appear edematous, they are actually obese, and diuretic therapy is rarely necessary. Our therapy has consisted of providing maintenance fluids intravenously, ventilatory assistance if needed, and correction of hypoglycemia and hypocalcemia. Echocardiography has proved useful in identifying hypertrophic cardiomyopathy and in identifying other forms of congenital heart disease. In view of the mild hypertrophy found in the asymptomatic IDMs, routine screening by echocardiography is unnecessary for these infants.

Acknowledgment

We thank Dr. Dan G. McNamara for his review of the manuscript. Linda Kaufman and Paula Kligman performed the echocardiograms.

References

Ethmozin, A New Antiarrhythmic Drug for Suppressing Ventricular Premature Complexes

PHILIP J. PODRID, M.D., ANATOLI LYAKISHEV, M.D., BERNARD LOWN, M.D., AND NICHOLAI MAZUR, M.D.

SUMMARY Ethmozin, a phenothiazine derivative, is an antiarrhythmic drug synthesized in the USSR. Preliminary data suggest that it is effective against a diversity of ectopic arrhythmias. The present study, carried out in the USSR, was designed to assess efficacy and patient tolerance of this new drug. Thirty-seven patients with chronic, persistent, frequent and symptomatic ventricular premature complexes (VPCs) were studied. VPCs were exposed by means of 24-hour ambulatory monitoring and exercise stress testing. Two drug schedules were used. Group 1, consisting of 11 patients, received 225 mg/day of ethmozin, while group 2, consisting of 26 patients, received 600 mg/day. Acute drug testing with a single large dose of ethmozin was followed by multiple dosing for a minimum of 4 days. Placebo was given in a single-blind fashion only to responders.

Only two patients in group 1 had a significant reduction in VPCs as evaluated by both monitoring and exercise testing. Fourteen patients in group 2 (54%) showed striking suppression of VPCs. Mild and transient effects were encountered in only four of the 37 patients. We conclude that ethmozin appears to be a well-tolerated, relatively effective agent for controlling VPCs.

PATIENTS with ventricular arrhythmias are being detected in increasing numbers because of the widespread use of ambulatory monitoring and exercise stress testing. Currently available antiarrhythmic drugs, however, are not consistently effective, safe, or well tolerated. There is an urgent need for drugs that suppress ventricular arrhythmias, cause minimal adverse reactions and have a prolonged duration of action so as to gain patient acceptance and adherence.

In 1965, the Institute of Pharmacology of the USSR Academy of Medical Sciences synthesized a new antiarrhythmic drug, ethmozin, the hydrochloride of 10-(3-morpholinopropionyl)-phenothiazine-2-carboxylic acid, ethylester (fig. 1). Early reports in the USSR have shown that ethmozin effectively controls ventricular and supraventricular arrhythmias in experimental animals and in man.1-4 However, these studies were not completely persuasive, because the evaluation of drug efficacy was based exclusively on brief electrocardiographic records and the reports of patients. In the USA, Danilo et al.9 showed that ethmozin possesses lidocaine-like properties on isolated Purkinje fibers. Morganroth and coworkers,10 in preliminary clinical investigations, have found the drug to be effective and induce few adverse reactions.

These promising results with ethmozin invited further clinical investigations using currently available technology. Using protocols for acute and chronic antiarrhythmic drug testing developed and used in the cardiovascular laboratories at the Harvard School of Public Health,11-14 a joint study of patients with frequent ventricular premature complexes (VPCs) was conducted in Moscow in 1977. Because the aim was to establish drug efficacy for suppressing ventricular arrhythmias and to assess patient tolerance, the group studied was recruited exclusively on the basis of VPC frequency and included subjects both with and without heart disease.

Material and Methods

Thirty-seven patients with frequent ventricular ectopic activity constituted the study population. There
Characterization of the cardiomyopathy in infants of diabetic mothers.
H P Gutgesell, M E Speer and H S Rosenberg

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