Epidemiology of Idiopathic Cardiomyopathies in Children and Adolescents
A Nationwide Study in Finland

Anita Arola, Eero Jokinen, Olli Ruuskanen, Markku Saraste, Erkki Pesonen, Anna-Leena Kuusela, Tero Tikanoja, Terho Paavilainen, and Olli Simell

Although idiopathic cardiomyopathies are prognostically important and are a common indication for cardiac transplantation in all age groups, the incidence and age distribution of idiopathic cardiomyopathies in a well-defined pediatric population have been poorly characterized. A retrospective study was carried out in Finland in 1980–1991 to obtain information on the epidemiology of childhood cardiomyopathies. The medical records of all patients aged birth to 20 years with cardiomyopathy from the five university hospitals and 16 central hospitals covering the entire country were reviewed. Moreover, data on causes of death from the Finnish National Census Bureau were examined. Of the 808 potential cases screened, 118 infants, children, and adolescents, representing an average age-specific population of 1.4 million, were definitely identified as having idiopathic cardiomyopathy. The average annual occurrence of new cases was 0.65 per 100,000 population (95% confidence interval (CI) 0.53–0.79). If the 15 cases diagnosed only after death during the 12-year study period were included, the occurrence increased to 0.74 per 100,000 population per year. Fifty-six new cases of dilated cardiomyopathy and 40 new cases of hypertrophic cardiomyopathy were diagnosed during the study period, giving average annual occurrences of 0.34/100,000/year (95% CI 0.26–0.44) and 0.24/100,000/year (95% CI 0.17–0.33) for new cases of dilated and hypertrophic cardiomyopathies, respectively. At the end of 1991, the prevalence of dilated cardiomyopathy was 2.6/100,000 (95% CI 1.8–3.6) and that for hypertrophic cardiomyopathy was 2.9/100,000 (95% CI 2.0–4.0). The number of new cases of dilated cardiomyopathy per year increased over the study period, whereas the annual occurrence of hypertrophic cardiomyopathy remained relatively constant. Marked variability was seen in occurrence among the different age groups of children with dilated cardiomyopathy, suggesting that different pathophysiologic mechanisms, and possibly etiologies, may exist in different age groups. Am J Epidemiol 1997;146:385–93.

Cardiomyopathies are a heterogeneous group of myocardial diseases with multifactorial etiologies. In recent decades, the introduction of endomyocardial biopsy and advances in molecular biologic techniques have greatly increased our knowledge of the etiology and pathogenesis of cardiomyopathies. However, many cardiomyopathies must still be classified as idiopathic (1). They cause marked morbidity as well as mortality and are an important indication for heart transplantation in all age groups. Very little can be done in terms of primary prevention at present.

The spectrum of cardiomyopathies in children differs from that in adults. Endocardial fibroelastosis is almost exclusively diagnosed in childhood (2), whereas the diagnosis of hypertrophic cardiomyopathy is often delayed until adolescence or early adulthood (3). Although cardiomyopathies have multifactorial etiology in both children and adults, genetic defects may play a more important role in infants and children (4), whereas environmental factors become increasingly important towards adulthood (1).

Numerous recent studies carried out in children have focused on the diagnosis and prognosis of car-
diomyopathies (5–9), but only a few reports have been published on their epidemiology during the era of modern diagnostic methods and currently accepted definitions (10, 11). We have carried out a retrospective study with strict inclusion and exclusion criteria for the cases in order to evaluate the epidemiology of idiopathic cardiomyopathies in a well-defined population and to obtain information on the age-specific occurrences of various types of cardiomyopathy in children.

MATERIALS AND METHODS

Patients

All patients aged birth to 20 years diagnosed in 1980–1991 as having cardiomyopathy or followed up because of a history of cardiomyopathy were identified from the medical records of the five university hospitals in Finland, where the treatment of pediatric patients with cardiomyopathy is centered. To ensure maximum certainty about case identification, we reviewed the records not only of all patients given the diagnosis of cardiomyopathy (code 425) but also of all patients given the diagnosis of undefined arrhythmia (code 427), heart failure of unknown origin (code 428), or an unspecified pathologic cardiac condition such as cardiac enlargement, as well as cardiac myodegeneration of unknown origin (code 429), from the Finnish version of the International Classification of Diseases (ICD), Eighth (12) and Ninth (13) Revisions. To include cases diagnosed and followed up at the central hospital level only, we contacted every physician responsible for children and adolescents with cardiac problems at the 16 central hospitals, with subsequent review of the medical records of all potential cases. Furthermore, we examined the files of the Finnish National Census Bureau, which records every death certificate in the country, to identify patients with cardiomyopathy whose disease was diagnosed only after death. Demographic data were obtained from the national Statistical Abstract of Finland. The study protocol was accepted by the Joint Commission on Ethics of Turku University and Turku University Central Hospital, as well as the Ministry of Social Affairs and Health.

The evaluation of patients had included a thorough medical history, physical examination, standard blood chemical analysis and hematologic measurements, electrocardiography, chest radiography, and echocardiography and/or heart catheterization. Initial diagnosis was based on echocardiography alone in 60 patients (51 percent), on echocardiography and catheterization in 52 patients (44 percent), on catheterization and angiocardiology in four patients (3.4 percent), and on autopsy in one patient. In a few cases, various diagnostic procedures and repeated examinations were required before a correct diagnosis was obtained. Specific causes of myocardial disease were excluded using metabolic screening, including serum carnitine measurements, and tests for identification of specific infective agents and immunologic disturbances. Skeletal muscle biopsy was carried out only in selected patients, as were biochemical analysis of mitochondrial enzyme activities and tests for identification of defects in mitochondrial DNA in myocardial and/or skeletal muscle specimens.

The Finnish National Census Bureau data on deceased patients included the age and sex of the patient as well as the year of cardiomyopathy death. The Eighth Revision of the ICD (12), used in Finland until the end of 1986, did not distinguish between dilated (i.e., congestive), hypertrophic, and restrictive cardiomyopathies. Therefore, data on the specific type of cardiomyopathy could be obtained only from 1987 onward, when the Ninth Revision of the ICD (13) was introduced in Finland.

Diagnostic criteria

The patients in the study were categorized mainly according to the guidelines of the World Health Organization/International Society and Federation of Cardiology Task Force on Cardiomyopathies (14), with the exception that primary endocardial fibroelastosis as a component of dilated or restrictive cardiomyopathies was also included. The question of the role of endocardial fibroelastosis among cardiomyopathies is controversial. No consensus prevails as to whether endocardial fibroelastosis is a primary phenomenon with secondary myocardial involvement or a reactive change following myocardial abnormality (2, 15). However, recent studies have tended to consider endocardial fibroelastosis as an expression of dilated cardiomyopathy, because the clinical and echocardiographic findings in the more common dilated form of endocardial fibroelastosis cannot be distinguished from dilated cardiomyopathy (9).

Patients with dilated cardiomyopathy showed dilatation of the left cardiac ventricle, the right cardiac ventricle, or both, with impaired systolic function (14). The left ventricular end-diastolic and end-systolic dimensions were at least 2 standard deviations (SDs) greater than those established for a normal heart according to age and body surface area, and left ventricular ejection fraction or fractional shortening was at least 2 SDs below that in normal subjects (≤55 percent and ≤0.26, respectively) (16). Because of the known difficulty of differentiating between myocarditis and dilated cardiomyopathy on a clinical basis,
patients without a histologic diagnosis were included only if the left ventricular size or function, or both, remained abnormal for at least 6 months.

In hypertrophic cardiomyopathy, the walls of the left ventricle were persistently thickened without any known stimulus to hypertrophy (14). The hypertrophy was either asymmetric or concentric. Absolute thickness of the interventricular septum or the left ventricular free wall, or both, exceeded by at least 2 SDs the normal values according to the age and body surface area of the patient (16).

Restrictive cardiomyopathy was recognized on the basis of abnormal ventricular filling during diastole (17, 18). Doppler echocardiography showed typical rapid completion of filling of the left ventricle in early diastole with little or no further filling in late diastole (17). The diagnosis was supported by normal or small ventricular volume and by secondary increases in atrial dimensions due to increased filling pressures of the ventricles.

Endocardial fibroelastosis was diagnosed when light microscopy showed a thickened endocardium consisting of excess fibrous tissue and abundant elastic fibers, as shown by elastic tissue stains. The thickened endocardium localized to the left ventricle alone or more diffusely in all cardiac chambers.

A definitive diagnosis of arrhythmogenic right ventricular dysplasia or cardiomyopathy was made by histologic demonstration of transmural fibrous and/or adipose tissue replacement of the right ventricular myocardium (19). The clinical criteria used in the absence of a histologic diagnosis included structural or functional abnormalities of the right ventricle, certain repolarization and depolarization abnormalities, conduction abnormalities, ventricular arrhythmias, and a positive family history (19).

All patients with hemodynamically significant structural heart defects, primary pulmonary or systemic hypertension, ischemic myocardial injury, systemic or metabolic disorders with potential myocardial involvement, neuromuscular diseases, a history of treatment with antineoplastic agents, or cardiomyopathy probably resulting from primary arrhythmia were excluded from the study.

Data analysis

Average annual occurrences were calculated with the observed number of new cases of cardiomyopathy divided by the arithmetic mean of the number of individuals in groups of the same age and sex among the Finnish general population for each year in 1980–1991. Point prevalences for dilated cardiomyopathy, hypertrophic cardiomyopathy, and all cardiomyopathies were calculated by dividing the total number of cases of cardiomyopathy by the number of individuals in the age-specific population on December 31, 1991. Ninety-five percent confidence intervals were estimated from the Poisson distribution (20). All p values less than or equal to 0.05 were considered statistically significant.

RESULTS

Using hospital records, 808 infants, children, and adolescents who fulfilled the selection criteria of the study were found in the period 1980–1991. Of these, 118 were judged to have idiopathic cardiomyopathy. There were 107 newly diagnosed cases, whereas 11 of the cases had been diagnosed before 1980 and were thus included only in the prevalence rates. The Finnish National Census Bureau mortality data contained 15 cardiomyopathy deaths which had not been found using the hospital charts; on the other hand, nine deaths recorded by the hospitals were missing from the Census Bureau database. Because of the lack of essential information on the 15 deceased patients from the Census Bureau data, these patients were included in the final calculations as “probable” cases of cardiomyopathy.

Dilated cardiomyopathy was the most common form of cardiomyopathy, diagnosed in 62 patients (52 percent), 12 of whom had endocardial fibroelastosis. Forty-four individuals (37 percent) had hypertrophic cardiomyopathy. Restrictive cardiomyopathy was identified in six patients and arrhythmogenic right ventricular dysplasia in three patients. Three patients could not be readily classified into any of these categories. The average annual occurrence of firmly established new cases of cardiomyopathy was thus 0.65 per 100,000 population (95 percent confidence interval (CI) 0.53–0.79) (table 1). When the “probable” cases of cardiomyopathy were included, the occurrence increased to 0.74/100,000/year (95 percent CI 0.62–0.89). Thus, 9–10 new cases of cardiomyopathy were diagnosed in Finnish hospitals each year, and 1–2 additional cases were disclosed only after postmortem examination. On December 31, 1991, 82 patients had idiopathic cardiomyopathy in an age-specific population of 1,336,377, resulting in a prevalence of 6.1/100,000 (95 percent CI 4.9–7.6). The cases showed an even geographic distribution; i.e., there was neither any accumulation of cases in certain parts of the country nor any difference in frequencies between patients from urban areas and their rural counterparts.

Dilated cardiomyopathy

Based on 56 new cases (28 males and 28 females) of dilated cardiomyopathy, the average annual occur-
Dilated cardiomyopathy

<table>
<thead>
<tr>
<th>Type of cardiomyopathy and age (years)</th>
<th>No. of males</th>
<th>No./100,000</th>
<th>No. of females</th>
<th>No./100,000</th>
<th>Total no.</th>
<th>Total occurrence</th>
</tr>
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<tbody>
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<td>&lt;1</td>
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<td>1–5</td>
<td>9</td>
<td>0.46</td>
<td>5</td>
<td>0.27</td>
<td>14</td>
<td>0.37</td>
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<tr>
<td>6–10</td>
<td>1</td>
<td>0.051</td>
<td>2</td>
<td>0.11</td>
<td>3</td>
<td>0.078</td>
</tr>
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<td>11–15</td>
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<td></td>
<td>2</td>
<td>0.052</td>
</tr>
<tr>
<td>16–20</td>
<td>7</td>
<td>0.33</td>
<td>1</td>
<td>0.049</td>
<td>8</td>
<td>0.19</td>
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<tr>
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<td>28</td>
<td>0.33</td>
<td>28</td>
<td>0.35</td>
<td>56</td>
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Hypertrophic cardiomyopathy

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<tr>
<th>Type of cardiomyopathy and age (years)</th>
<th>No. of males</th>
<th>No./100,000</th>
<th>No. of females</th>
<th>No./100,000</th>
<th>Total no.</th>
<th>Total occurrence</th>
</tr>
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<td></td>
<td>2</td>
<td>0.26</td>
</tr>
<tr>
<td>1–5</td>
<td>5</td>
<td>0.26</td>
<td>3</td>
<td>0.16</td>
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<td>5</td>
<td>0.26</td>
<td>1</td>
<td>0.054</td>
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<td>0.16</td>
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<tr>
<td>11–15</td>
<td>9</td>
<td>0.46</td>
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<td>0.11</td>
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<td>0.28</td>
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<tr>
<td>16–20</td>
<td>9</td>
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<td>4</td>
<td>0.20</td>
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<tr>
<td>Total</td>
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<td>0.36</td>
<td>10</td>
<td>0.12</td>
<td>40</td>
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All cardiomyopathy

<table>
<thead>
<tr>
<th>Type of cardiomyopathy and age (years)</th>
<th>No. of males</th>
<th>No./100,000</th>
<th>No. of females</th>
<th>No./100,000</th>
<th>Total no.</th>
<th>Total occurrence</th>
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</thead>
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<td>10</td>
<td>0.53</td>
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<tr>
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<td>0.61</td>
<td>3</td>
<td>0.16</td>
<td>15</td>
<td>0.39</td>
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<td>16–20</td>
<td>16</td>
<td>0.76</td>
<td>5</td>
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<td>0.51</td>
</tr>
<tr>
<td>Total</td>
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<td>0.77</td>
<td>42</td>
<td>0.52</td>
<td>107</td>
<td>0.65</td>
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</table>

* Age- and sex-specific occurrences are shown as absolute numbers of cases and per 100,000 population.
† CI, confidence interval.
‡ Includes five patients with restrictive cardiomyopathy, three patients with arrhythmogenic right ventricular dysplasia, and three patients with undefined cardiomyopathy.

The average annual occurrence of dilated cardiomyopathy increased from 0.25/100,000 to 0.44/100,000 between the first (1980–1985) and second (1986–1991) halves of the study period (p = 0.048) (table 2). Interestingly, the occurrence (prevalence) in infants increased 2.7-fold, from 2.1/100,000/year to 5.6/100,000/year (p = 0.022) (table 2). The proportion of endocardial fibroelastosis in all patients with dilated cardiomyopathy remained relatively constant, whereas a decreasing, statistically nonsignificant tendency was seen among infants, accounting for 50 percent and 29 percent of dilated cardiomyopathies during the first and second halves of the study period, respectively.

The symptoms of patients with dilated cardiomyopathy at the time of diagnosis ranged from symptoms of congestive heart failure (n = 55; 89 percent) to asymptomatic situations (n = 7; 11 percent) (table 3). The symptoms had gradually developed over weeks or even months in 28 patients (45 percent). The most common preceding symptoms in infants consisted of feeding difficulties, poor weight gain, and abnormal sweating, whereas older children and adolescents had typically suffered from a gradual loss of physical performance capacity with progressive respiratory distress and fatigue. Nineteen patients (31 percent) had a history of infectious disease in the near past (≤3

<table>
<thead>
<tr>
<th>Type of cardiomyopathy and study period</th>
<th>No. of patients</th>
<th>Disease occurrence*</th>
<th>p value</th>
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<td>Dilated cardiomyopathy</td>
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<td></td>
</tr>
<tr>
<td>All patients</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>1980–1985</td>
<td>21</td>
<td>0.25</td>
<td></td>
</tr>
<tr>
<td>1986–1991</td>
<td>35</td>
<td>0.44</td>
<td>0.048</td>
</tr>
<tr>
<td>Infants†</td>
<td></td>
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</tr>
<tr>
<td>1980–1985</td>
<td>8</td>
<td>2.1</td>
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<tr>
<td>1986–1991</td>
<td>21</td>
<td>5.6</td>
<td>0.022</td>
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<tr>
<td>Hypertrophic cardiomyopathy</td>
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<td></td>
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<tr>
<td>All patients</td>
<td></td>
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<td></td>
</tr>
<tr>
<td>1980–1985</td>
<td>22</td>
<td>0.25</td>
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</tr>
<tr>
<td>1986–1991</td>
<td>18</td>
<td>0.22</td>
<td>NS†</td>
</tr>
<tr>
<td>Infants†</td>
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<tr>
<td>1980–1985</td>
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<td>0</td>
<td></td>
</tr>
<tr>
<td>1986–1991</td>
<td>2</td>
<td>0.26</td>
<td>NS</td>
</tr>
</tbody>
</table>

* Average number of new cases per 100,000 age-specific population per year.
† Patients under 1 year of age.
‡ NS, not significant.


<table>
<thead>
<tr>
<th>Symptom</th>
<th>No.</th>
<th>%</th>
</tr>
</thead>
<tbody>
<tr>
<td>Congestive heart failure</td>
<td>55</td>
<td>89</td>
</tr>
<tr>
<td>Arrhythmias and/or conduction disturbances</td>
<td>13</td>
<td>21</td>
</tr>
<tr>
<td>Chest pain</td>
<td>2</td>
<td>3.2</td>
</tr>
<tr>
<td>Asymptomatic†</td>
<td>7</td>
<td>11</td>
</tr>
</tbody>
</table>

* A single patient often had multiple major symptoms at presentation.
† Includes four patients with systolic murmur and/or cardiac enlargement on the chest radiograph, two patients with a history of heart failure during respiratory infection in infancy, and one patient with recurrent infections.

months before diagnosis). Nine patients (14 percent) had signs and symptoms of respiratory tract infection, and one had a urinary tract infection at presentation. No definite seasonal or month-to-month variation was found in either time of diagnosis or onset of the first symptoms of the preceding infection. Cardiac tissue was available from 33 patients (53 percent) for histopathologic examination. Endomyocardial biopsy specimens were obtained from nine patients (14 percent) a median of 2 months (range, 2 weeks to 13 months) after clinical presentation; four patients (6.4 percent) underwent heart transplantation; and autopsy was carried out in 29 patients (47 percent). In all of these patients, myocarditis, defined retrospectively by the Dallas criteria (21), could be excluded as a possible cause of a dilated, poorly con-
abiotic defect. In seven children (16 percent), hypertrophic cardiomyopathy was associated with a syndrome.

Restrictive cardiomyopathy

Six male patients had restrictive cardiomyopathy; four of them presented with congestive heart failure. The patients’ ages at diagnosis varied from 2 years to 14 years (median, 7.2 years). A significant diagnostic delay occurred between the first cardiac symptoms or signs and correct diagnosis, varying from 2 weeks to 6 years (median, 12 months). Remarkably, all but one of the cases were diagnosed after 1987, possibly reflecting the relative unfamiliarity of clinicians with the disease and the less advanced diagnostic equipment available during the first half of the study period.

Arrhythmogenic right ventricular dysplasia

Only three patients had arrhythmogenic right ventricular dysplasia. The patients were 9, 13, and 15 years of age at the time of diagnosis; in one, the diagnosis was made postmortem. All patients had suffered from syncopal seizures during physical exercise. Two patients had treatment-resistant ventricular tachycardias, and one had ventricular and supraventricular extrasystoles, conduction disturbances, and bradyarrhythmias. One of the patients had the familial form of the disease. A significant diagnostic delay (from 8 months to >4 years) from the first appearance of symptoms to correct diagnosis was also seen in this group.

DISCUSSION

The present study, which used clearly defined criteria and modern diagnostic methods, offers reasonable estimates of the occurrence of idiopathic cardiomyopathies in pediatric and adolescent age groups. Moreover, several factors favor the results obtained from epidemiologic studies carried out in Finland. First, the Finnish population of 5.1 million is racially homogeneous, and the various units of the health care system—i.e., well-baby clinics, health care centers, and district, central, and university hospitals—are easily accessible to everyone. Second, the diagnosis and treatment of patients with cardiomyopathy in pediatric age groups are centered in university hospitals. We reviewed the original inpatient and outpatient clinical records of every patient with cardiomyopathy from the five university hospitals, and to achieve maximum certainty regarding case identification, we screened many ill-defined cardiac diagnoses for cardiomyopathy. Moreover, one of the authors (A.A.) contacted every physician responsible for children and adolescents with cardiac problems at the 16 central hospitals so that we could include the patients who had been followed up at the central hospital level only. To check the reliability of the identification of cases, we reviewed age- and sex-specific data on deaths caused by cardiomyopathy from the Finnish National Census Bureau.

Although this study was, strictly speaking, based on referred patients, it was very close to a population-based study, with almost complete case ascertainment. In only four patients (3.4 percent) was the diagnosis of cardiomyopathy made at the central hospital level. Moreover, the finding that almost one third of the patients (n = 34; 29 percent) were asymptomatic at presentation indicates that not only the most advanced cases are seen at the university hospitals in Finland. The National Census Bureau data included 15 deaths that were not found in the clinical records, suggesting that the diagnosis was made only after death in these patients. At the same time, however, a few patients with a definite diagnosis of cardiomyopathy who died during follow-up were found in the hospital charts but were missing from the Census Bureau data, indicating that the Census Bureau was not notified of all cases or, alternatively, that these cases were registered as having died of infections and/or arrhythmias which often precede death in these patients.

In the present study, the values for average annual occurrence (0.65/100,000) and prevalence (6.1/100,000) of childhood cardiomyopathies are probably slight underestimates of the true values, since we used strict echocardiographic criteria, accepting only patients with a definite diagnosis of cardiomyopathy.
Epidemiology of Childhood Cardiomyopathies

The finding is at least partly explainable by the use and accuracy of echocardiographic techniques and the more accurate diagnoses resulting from increasing explained by the study protocols, relatively small for the lack of children with cardiomyopathy in those study populations, or even geographic differences in the occurrence of cardiomyopathies.

Most earlier studies in children were carried out before the development of modern echocardiographic techniques or were limited by a lack of specific diagnostic criteria. It is therefore difficult to compare results from those studies with those of the present study. Moreover, the relative infrequency of idiopathic cardiomyopathies, their potentially multifactorial etiology, and the fact that the mechanisms of myocardial damage in most cases remain largely unknown have made this and other epidemiologic studies, especially retrospective ones, difficult to perform. The moment of initial myocardial insult is often impossible to determine, and the amount of time from that moment to the appearance of the first symptoms and signs of cardiomyopathy may be days, weeks, or years, possibly depending on the etiology of the cardiomyopathy as well as the age and genetic and immunologic status of the patient. The prevalence of 10/100,000 for all cardiomyopathies in infancy which was reported by Ferencz and Neill is clearly higher than the 3.8/100,000/year seen in the present study. The discrepancy probably reflects differences in the definition and in inclusion criteria. The study by Gillum, although based on hospital discharge statistics and therefore not directly comparable with the present study, reported a discharge rate of 3.9/100,000 for dilated and hypertrophic cardiomyopathies in children under 15 years of age in 1982, a value highly similar to the prevalence of 4.7/100,000 for all cardiomyopathies obtained in the present study in 1991 (data not shown). On the other hand, there have been several studies of all age groups that did not identify any pediatric cases (10, 11, 25). The reason for the lack of children with cardiomyopathy in those studies is unknown, but the finding could possibly be explained by the study protocols, relatively small study populations, or even geographic differences in the occurrence of cardiomyopathies.

The results of this study and of previous studies (11) suggest that the incidence of cardiomyopathies is increasing. The finding is at least partly explainable by the more accurate diagnoses resulting from increasing use and accuracy of echocardiographic techniques and by a higher index of suspicion among clinicians, although a true increase in incidence may be possible. In the present study, the increase in the occurrence of cardiomyopathies over time was mainly found to be due to an increase in the number of new cases of dilated cardiomyopathy and was most prominent in infants, especially neonates. The high neonatal occurrence may reflect immature myocardial metabolism and restricted hemodynamic compensatory mechanisms typical in this age group; on the other hand, this age group showed the greatest tendency to recover (data not shown). The average annual occurrence of hypertrophic cardiomyopathy remained relatively constant in the present analysis. Our finding differs from that obtained in a recent study by Codd et al. (11), in which a marked increase over time was observed in adults. The discrepancy between these two studies may simply reflect the fact that diagnostic practices applied to children are different from those applied to adults.

Myocarditis may cause dilatation and hypokinesia of the left ventricle and thus may resemble idiopathic dilated cardiomyopathy. Ideally, myocarditis should be ruled out in patients with dilated cardiomyopathy. In practice, however, endomyocardial biopsy is not routinely performed in all patients with a dilated and poorly contracting left ventricle, because of 1) a tendency toward spontaneous recovery in many patients, 2) the known risks of biopsy in infants, 3) possible sampling errors associated with biopsy, and 4) the fact that no specific treatment is available. Inflammatory changes have been found by endomyocardial biopsy in up to 67 percent of patients with dilated cardiomyopathy, depending on the amount of time from onset of symptoms to biopsy. However, the mechanisms by which myocarditis, commonly caused by viruses, possibly develops into chronic myocardial disease are largely unknown. The virus may persist in the myocardium or may lead to cardiomyopathy via virus-induced autoimmune mechanisms in a genetically predisposed individual. In the present study, 40 percent of patients with dilated cardiomyopathy had symptoms of respiratory or gastrointestinal infection just before diagnosis or at diagnosis. However, the role of viral infection in the natural history of cardiomyopathy could not be established—i.e., whether a potentially cardiotropic virus initiated the myocardial disease process in a predisposed individual or simply unmasked a latent cardiomyopathic diathesis. Histopathologic examination of biopsy specimens, as well as myocardial samples obtained from heart transplantation or autopsy, excluded myocarditis in 53 percent of patients with dilated cardiomyopathy, although possible resolution...
of the myocarditic changes over time (32) could not be ruled out in the majority of these cases.

In the present study, familial hypertrophic cardiomyopathy was identified or suspected from the family history in 57 percent of the patients. A relatively great number of sporadic cases may be explained by the fact that the families were not systematically studied. The marked male preponderance (male:female ratio 3:1) noticed in this study and a similar recent finding in adults (41) suggest that, in addition to the proposed autosomal-dominant inheritance of hypertrophic cardiomyopathy in these populations (42–45), other mechanisms may also be involved (46). The influence of male sex or other factors, such as genomic imprinting (47), on the penetrance and phenotype of hypertrophic cardiomyopathy remain to be elucidated.

In conclusion, this nationwide study offers a reasonable estimate of the occurrence of dilated and hypertrophic cardiomyopathies in children and adolescents in a well-defined population. The information may be helpful in choosing treatment strategies, including heart transplantation, for these patients. A marked difference in the annual occurrence of new cases of dilated cardiomyopathy between infants and older children suggests that different pathophysiologic mechanisms, and possibly etiologies, are involved in the different age groups. Clearly, inheritance has a significant role in the etiology of both dilated and hypertrophic cardiomyopathies, although the specific mechanisms involved remain to be further evaluated.

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