Echocardiographic assessment of the evolution of amyloid heart disease: a study with familial amyloid polyneuropathy

MINORU HONGO, M.D., AND SHU-ICHI IKEDA, M.D.

ABSTRACT To determine the evolution of amyloid heart disease, 28 patients with familial amyloid polyneuropathy (FAP) were studied by echocardiography. The incidence and degree of the abnormalities were correlated with the neurologic disabilities, duration of the illness, and age in cross-sectional studies. Serial studies were performed in 12 patients, who were followed for a mean of 27.7 months. At the initial examinations, left ventricular diastolic function was reduced in six patients, while systolic function was preserved in eight. On follow-up there occurred significant increases in ventricular septal wall thickness (from 10.7 ± 3.1 to 13.1 ± 3.2 mm; p < .01) and posterior wall thickness (from 11.8 ± 2.5 to 13.5 ± 2.3 mm; p < .01), and reductions in the E-F slope of the mitral valve (from 64.4 ± 18.8 to 43.9 ± 11.0 mm/sec; p < .01), percent fractional shortening (from 36.5 ± 9.4% to 28.8 ± 8.2%; p < .02), and left ventricular internal diastolic dimension (from 46.2 ± 6.1 to 42.4 ± 6.2 mm; p < .001). At the final examinations, marked ventricular hypertrophy was found in three patients, reduced left ventricular diastolic function in all, impaired systolic function in nine, and decreased left ventricular internal dimension in three. In addition, highly refractile myocardial echoes had appeared in two patients, pericardial effusion in three, and valve thickening in two. We conclude that amyloid heart disease in patients with FAP develops slowly but progressively.


RECENTLY many echocardiographic studies on amyloid heart disease1-8 have been reported. Usually the cardiac involvement has been severe with gross changes including marked thickening of left and right ventricular walls, normal or decreased left ventricular internal dimension, reduced left ventricular diastolic function, and often severe abnormalities of systolic function as well as valve thickening and pericardial effusion. Furthermore, hyperrefractile myocardial echoes on the two-dimensional echocardiographic images were reported to be characteristically diagnostic of amyloid heart disease.3,5,7,8 To our knowledge, however, these studies have mainly been cross-sectional ones of patients with far-advanced nonhereditary primary or senile amyloidosis and amyloidosis associated with myeloma, and the natural course of cardiac amyloidosis appears not to have been investigated hitherto by serial study.

The purpose of the present study was to determine the evolution of amyloid heart disease, by means of cross-sectional and serial echocardiographic studies, in patients with familial amyloid polyneuropathy (FAP),9-14 which is a hereditary systemic amyloidosis with chronic progression.

Methods

Subjects. During the past 8 years we examined 28 patients with FAP (14 men and 14 women, ages 33 to 67 years, mean 49.6 ± 10.2) from several locations in Nagano Prefecture12-14 in the central part of Japan. The diagnosis of FAP was based on neurologic findings and the confirmation of amyloid deposition in biopsy specimens (stomach, rectum, sural nerve, endomyocardium, skin, and kidney) or autopsy. All patients had chest roentgenographic, electrocardiographic, and both M mode and two-dimensional echocardiographic studies, and correlations between echocardiographic findings and the degree of the neurologic disabilities,11 duration of the illness, and age were examined. Neurologic disabilities were as follows: stage I, peripheral neuropathy limited to the lower limbs; stage II, neuropathy involving both the lower and upper limbs; stage III, bedridden because of extensively progressive neuropathy. Twelve patients (seven men and five women) were followed for 6 to 52 months
Echocardiographic studies. The instruments used were
electric sector scanners (Toshiba, model SSH-40A or SSH-11A
Sonolayergraph with 2.4 and 3.5 MHz transducers) or a
mechanical sector scanner (Aloka, model SSD-110S with 2.25
MHz transducer). The following variables were measured in
the M mode echocardiographic study: left ventricular internal end-
diastolic and end-systolic dimension, the interventricular septal
wall thickness (IVST) and the left ventricular posterior wall
thickness (PWT) at end-diastole, E-F slope of the anterior mitral
valve, and the right ventricular anterior wall thickness at end-
diastole (RVAVWT). Each variable was measured according to
the criteria recommended by the American Society of Echocar-
diography.\textsuperscript{15} In patients whose electrocardiograms showed si-
nus rhythm, we also measured the maximal diastolic endocar-
dial velocity (DEVM) of the posterior wall by the method
described by Kovick et al.\textsuperscript{16} Next, percent fractional shortening
(\%FS) and mean normalized velocity of circumferential fiber
shortening (mVcf) were calculated. In the two-dimensional
echocardiographic examination, in addition to normally discrimi-
inating cardiac structures, special attention was paid to highly
refractile myocardial echoes, the so-called granular sparkling
appearance, by parasternal, apical, and subxiphoid approaches.
Highly refractile echoes were defined as echoes that persisted at
gain settings low enough to completely eliminate the adjacent
echoes.

Statistical analysis. M mode echocardiographic data in the
serial studies were compared by paired and nonpaired t tests,
and statistical significance was assumed when the p value was
less than .05.

Results
Clinical presentation. Patients were classified neuro-
logically as follows: stage I, nine patients; stage II, 13; and
stage III, six. Duration of the illness from the onset of
symptoms ranged from 4 months to 30 years (0 to 5
years, eight patients; 5 to 10 years, 13; more than 10
years, seven; mean 8.1 ± 5.6 years). Thirteen of the
patients were over 50 years old. Clinically overt heart
disease was absent in 15 patients, and refractory con-
gestive heart failure and restrictive cardiomyopathy
were present in only three at the initial examinations.
None died of congestive heart failure during the fol-
low-up studies. Chest roentgenographic examination
revealed cardiac enlargement in seven patients and
pleural effusion in three. One or more electrocardio-
graphic abnormalities were found in 25 of the 28
patients.

Echocardiographic findings in the cross-sectional stud-
ies. As seen in tables 1, 2, and 3, the IVST, PWT, and
RVAVWT increased and the E-F slope, DEVM, \%FS,
mVcf, and left ventricular internal dimension de-
creased with the progression of the neurologic disabili-
ties, duration of the illness, and age. Highly refractile
granular sparkling echoes were observed in nine pa-
patients. All of them showed reductions in both the E-F
slope and DEVM; \%FS and mVcf were normal in five
(figure 1) and abnormal in the rest. Patients who
showed normal systolic function and an increased re-

\begin{table}
\centering
\begin{tabular}{|l|lll|}
\hline
 & \multicolumn{3}{c|}{Neurologic stage} \\
\hline
Measurements & I & II & III \\
\hline
IVST (mm) & 10.7±4.8 & 13.4±5.3 & 14.8±5.9 \\
&(n=7) & (n=12) & (n=5) \\
PWT (mm) & 11.3±2.7 & 12.9±3.0 & 14.0±4.3 \\
&(n=7) & (n=12) & (n=5) \\
RVAVWT (mm) & 5.0±1.9 & 5.1±2.4 & 11.5±2.5 \\
&(n=4) & (n=7) & (n=2) \\
LV \\
Ds (mm) & 46.1±5.7 & 45.8±6.4 & 44.0±6.5 \\
&(n=7) & (n=13) & (n=5) \\
%FS (%) & 38.9±9.4 & 34.9±8.3 & 34.1±10.9 \\
&(n=7) & (n=13) & (n=5) \\
mVcf (circ/sec) & 1.33±0.24 & 1.18±0.27 & 0.98±0.21 \\
&(n=7) & (n=12) & (n=5) \\
DEVM (mm/sec) & 100.8±28.0 & 83.7±8.0 & 76 \\
&(n=5) & (n=8) & (n=1) \\
MV \\
E-F slope (mm/sec) & 59.4±32.2 & 54.7±19.2 & 48.2±20.3 \\
&(n=9) & (n=12) & (n=6) \\
Incidence (%) & & & \\
GS & 22 & 31 & 50 \\
PE & 0 & 23 & 50 \\
\hline
\end{tabular}
\caption{Echocardiographic findings and neurologic disabilities (mean ± SD)}
\end{table}

fractile pattern in the myocardium had slightly greater
wall thickness (IVST, 13.4 ± 4.1 vs 9.8 ± 1.9 mm, p > .05; PWT, 13.2 ± 2.7 vs 11.1 ± 2.3 mm, p > .05)
than those who exhibited normal systolic function but
no refractile pattern. The incidences of the granular
sparkling echoes and pericardial effusion were higher in
neurologically severe, long-term, and elderly pa-
tients. No remarkable electrocardiographic finding
was observed in 10 of 15 patients without clinical
evidence of overt heart disease, but some echocardi-
ographic abnormalities were present in nine of them.
These included severe reduction in the E-F slope with-
out evidence of mitral valve thickening in six patients
(60\%) and significant decrease in the DEVM in seven
(70\%), whereas the \%FS and mVcf were normal in
most patients and the granular sparkling appearance
was observed in only one.

Echocardiographic findings in the serial studies. We fol-
lowed 12 patients, 10 of whom had one follow-up
study while the remaining two had two studies. Sig-
ificant increases in the IVST (from 10.7 ± 3.1 to
13.1 ± 3.2 mm; p < .01) and PWT (from 11.8 ± 2.5
to 13.5 ± 2.3 mm; p < .01), and reductions in the E-F

(mean 27.7 ± 13.8) and had serial echocardiographic studies.
TABLE 2  
Echocardiographic findings and duration of illness (mean ± SD) 

<table>
<thead>
<tr>
<th>Measurements</th>
<th>Duration of illness (yr)</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>0-5</td>
</tr>
<tr>
<td>IVST (mm)</td>
<td>8.7±1.6</td>
</tr>
<tr>
<td></td>
<td>(n = 6)</td>
</tr>
<tr>
<td>PWT (mm)</td>
<td>10.2±1.8</td>
</tr>
<tr>
<td></td>
<td>(n = 6)</td>
</tr>
<tr>
<td>RVAWT (mm)</td>
<td>4.1±0.1</td>
</tr>
<tr>
<td></td>
<td>(n = 2)</td>
</tr>
<tr>
<td>LV</td>
<td></td>
</tr>
<tr>
<td>Dd (mm)</td>
<td>47.7±5.8</td>
</tr>
<tr>
<td></td>
<td>(n = 6)</td>
</tr>
<tr>
<td>Ds (mm)</td>
<td>33.2±5.2</td>
</tr>
<tr>
<td></td>
<td>(n = 6)</td>
</tr>
<tr>
<td>%FS (%)</td>
<td>37.2±7.1</td>
</tr>
<tr>
<td></td>
<td>(n = 6)</td>
</tr>
<tr>
<td>mVcf (circ/sec)</td>
<td>1.25±0.20</td>
</tr>
<tr>
<td></td>
<td>(n = 6)</td>
</tr>
<tr>
<td>DEVM (mm/sec)</td>
<td>104.4±25.4</td>
</tr>
<tr>
<td></td>
<td>(n = 5)</td>
</tr>
<tr>
<td>MV</td>
<td></td>
</tr>
<tr>
<td>E-F slope (mm/sec)</td>
<td>59.8±14.1</td>
</tr>
<tr>
<td></td>
<td>(n = 8)</td>
</tr>
<tr>
<td>Incidence (%)</td>
<td></td>
</tr>
<tr>
<td>GS</td>
<td>13</td>
</tr>
<tr>
<td>PE</td>
<td>13</td>
</tr>
</tbody>
</table>

Abbreviations as in table 1.

slope (from 64.4 ± 18.8 to 43.9 ± 11.0 mm/sec; p < .01), DEVM (from 91.8 ± 28.4 to 75.0 ± 23.7 mm/sec; p < .05), %FS (from 36.5 ± 9.4% to 28.8 ± 8.2%; p < .02), mVcf (from 1.18 ± 0.25 to 0.92 ± 0.22 circumferences/sec; p < .01), left ventricular internal end-diastolic dimension (from 46.2 ± 6.1 to 42.4 ± 6.2 mm; p < .001), without significant change in end-systolic dimension, occurred during the follow-up studies (figures 2 and 4). The RVAWT, which could be identified in three patients, also increased from 3.7 ± 0.5 to 4.8 ± 0.2 mm. In two patients who had two follow-up studies, similar but gradual changes were observed in these variables during the first and the second studies (figure 4). In four patients in whom the %FS and mVcf were normal at the initial examinations but became abnormal in their last echocardiograms, a significant reduction in the E-F slope occurred (from 63.5 ± 5.4 to 43.0 ± 8.5 mm/sec; p < .05) (table 4). The other three patients had normal %FS and mVcf at the final examinations. Gradual reduction in the E-F slope occurred and the mean value at that time measured 47.0 ± 10.7 mm/sec (table 5). The granular sparkling echoes were newly observed in two patients (figure 3). As summarized in table 6, the IVST and PWT increased and the E-F slope, %FS, and mVcf decreased in both patients during the follow-up studies. Consequently, both had ventricular hypertrophy, severe reduction in the E-F slope, decrease in the DEVM, and abnormalities of the %FS and mVcf when highly refractile echoes were visualized. In the two-dimensional echocardiographic examinations, a small amount of pericardial effusion developed in three patients (figure 4) and a thickened mitral valve appeared in two, a thickened aortic valve in one, and thickened papillary muscles in three. The left atrium became enlarged in three patients and the right atrium in one.

Discussion

It is generally recognized that the cardiovascular system is commonly involved in systemic amyloidosis, usually presenting as refractory congestive heart failure.17-19 The diagnosis of amyloid heart disease is sometimes difficult, especially in nonhereditary cases, even after clinically significant cardiovascular symptoms occur because of marked clinical and hemodynamic similarities to other conditions such as restrictive cardiomyopathy and constrictive pericarditis. In contrast, FAP is a heredofamilial systemic amyloidosis with polyneuropathy, which shows chronic progression and variable degrees of amyloid infiltration.

TABLE 3  
Echocardiographic findings and age (mean ± SD) 

<table>
<thead>
<tr>
<th>Measurements</th>
<th>&lt;50</th>
<th>≥50</th>
</tr>
</thead>
<tbody>
<tr>
<td>IVST (mm)</td>
<td>10.1±2.9</td>
<td>15.9±6.1</td>
</tr>
<tr>
<td></td>
<td>(n = 12)</td>
<td>(n = 12)</td>
</tr>
<tr>
<td>PWT (mm)</td>
<td>11.3±2.5</td>
<td>14.2±3.6</td>
</tr>
<tr>
<td></td>
<td>(n = 12)</td>
<td>(n = 12)</td>
</tr>
<tr>
<td>RVAWT (mm)</td>
<td>3.8±1.1</td>
<td>7.9±3.5</td>
</tr>
<tr>
<td></td>
<td>(n = 6)</td>
<td>(n = 7)</td>
</tr>
<tr>
<td>LV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Dd (mm)</td>
<td>46.9±6.1</td>
<td>44.4±6.5</td>
</tr>
<tr>
<td></td>
<td>(n = 12)</td>
<td>(n = 13)</td>
</tr>
<tr>
<td>Ds (mm)</td>
<td>32.8±6.6</td>
<td>29.4±6.2</td>
</tr>
<tr>
<td></td>
<td>(n = 12)</td>
<td>(n = 13)</td>
</tr>
<tr>
<td>%FS (%)</td>
<td>39.1±8.1</td>
<td>32.4±9.5</td>
</tr>
<tr>
<td></td>
<td>(n = 12)</td>
<td>(n = 13)</td>
</tr>
<tr>
<td>mVcf (circ/sec)</td>
<td>1.29±0.23</td>
<td>1.01±0.22</td>
</tr>
<tr>
<td></td>
<td>(n = 12)</td>
<td>(n = 12)</td>
</tr>
<tr>
<td>DEVM (mm/sec)</td>
<td>100.1±22.5</td>
<td>76.2±4.9</td>
</tr>
<tr>
<td></td>
<td>(n = 7)</td>
<td>(n = 7)</td>
</tr>
<tr>
<td>MV</td>
<td></td>
<td></td>
</tr>
<tr>
<td>E-F slope (mm/sec)</td>
<td>59.2±18.0</td>
<td>48.8±20.0</td>
</tr>
<tr>
<td></td>
<td>(n = 15)</td>
<td>(n = 12)</td>
</tr>
<tr>
<td>Incidence (%)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>GS</td>
<td>27</td>
<td>39</td>
</tr>
<tr>
<td>PE</td>
<td>7</td>
<td>39</td>
</tr>
</tbody>
</table>

Abbreviations as in table 1.
FIGURE 1. M mode and two-dimensional echocardiograms obtained from a 54-year-old man (biopsy-proved cardiac amyloidosis) at the cross-sectional study. A, The interventricular septal wall and posterior wall are thickened. The maximal diastolic endocardial velocity of the posterior wall is markedly decreased, but %FS and mVcf are normal. B, Note a highly refractile appearance of the ventricular septum. L = left; R = right; A = anterior; P = posterior.

FIGURE 2. Serial M mode echocardiograms of the left ventricle in a 49-year-old woman with biopsy-proved amyloid heart disease. A, At the initial examination, significant decrease in the DEVM of the left ventricular posterior wall, normal IVST and PWT, and normal left ventricular internal dimension are observed. Left ventricular systolic function assessed by %FS and mVcf is preserved. B, At the final examination (46 months after the initial examination), significant increase in the wall thickness, decrease in the DEVM and left ventricular internal diastolic dimension, as well as marked abnormalities of systolic function are demonstrated.
normalities are not specific for cardiac amyloidosis and that absence of the two-dimensional granular sparkling appearance in no way rules out amyloid deposition in the myocardium, nor does its presence establish the diagnosis, since it can be seen in patients with hypertrophic cardiomyopathy and other infiltrative processes such as Pompe’s disease and hemochromatosis as well as in those with chronic renal failure.7

Serial echocardiographic studies were of value in assessing the evolution of amyloid heart disease. In our study, before clinically apparent heart disease developed, most patients without remarkable electrocardiographic changes already had some echocardiographic abnormalities. These included severe reduction in the E-F slope without evidence of mitral valve obstruction and significant decrease in the DEVM in common, whereas the %FS and mVcf were normal in most and the granular sparkling appearance was seen in only one. Thus reduction in left ventricular compliance16, 23 may be the first to develop in amyloid heart disease, although it is not possible to determine from our results whether a reduction in the E-F slope or a decrease in the DEVM is the first echocardiographic manifestation of increasing amyloid deposit. More frequent investigations on high-risk subjects or members of FAP families would perhaps clarify this problem.

Our follow-up studies lasted less than 3 years in most patients and some of them showed only slight changes during this period. However, there did occur significant increases in the IVST and PWT and reductions in the E-F slope, DEVM, %FS, mVcf, and end-diastolic dimension, and also a tendency for the RVAWT to increase. The degree of these M mode echocardiographic changes correlated generally with the follow-up period.

We attempted to analyze how well left ventricular systolic and diastolic function correlated before systol-

### Table 4

<table>
<thead>
<tr>
<th>Patient</th>
<th>%FS</th>
<th>mVcf (circ/sec)</th>
<th>E-F slope (mm/sec)</th>
<th>%FS</th>
<th>mVcf (circ/sec)</th>
<th>E-F slope (mm/sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>3</td>
<td>30</td>
<td>0.92</td>
<td>60</td>
<td>25</td>
<td>0.76</td>
<td>32</td>
</tr>
<tr>
<td>5</td>
<td>53</td>
<td>1.67</td>
<td>64</td>
<td>19</td>
<td>0.61</td>
<td>54</td>
</tr>
<tr>
<td>7</td>
<td>32</td>
<td>1.31</td>
<td>58</td>
<td>28</td>
<td>1.02</td>
<td>38</td>
</tr>
<tr>
<td>12</td>
<td>36</td>
<td>1.15</td>
<td>72</td>
<td>22</td>
<td>0.84</td>
<td>48</td>
</tr>
</tbody>
</table>

Significant reduction in the E-F slope of the mitral valve occurred in four patients in whom the %FS and mVcf were initially normal but became abnormal in the final examinations.

## Table 5

<table>
<thead>
<tr>
<th>Patient</th>
<th>%FS</th>
<th>mVcf (circ/sec)</th>
<th>E-F slope (mm/sec)</th>
<th>%FS</th>
<th>mVcf (circ/sec)</th>
<th>E-F slope (mm/sec)</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>48</td>
<td>1.49</td>
<td>95</td>
<td>47</td>
<td>1.43</td>
<td>59</td>
</tr>
<tr>
<td>4</td>
<td>53</td>
<td>1.39</td>
<td>95</td>
<td>39</td>
<td>1.08</td>
<td>33</td>
</tr>
<tr>
<td>10</td>
<td>40</td>
<td>1.36</td>
<td>58</td>
<td>38</td>
<td>1.24</td>
<td>49</td>
</tr>
</tbody>
</table>

The %FS and mVcf at the final examinations were normal in three patients. Gradual decrease in the E-F slope of the mitral valve occurred, which resulted in marked reduction at the final examinations.
ic abnormalities appeared. Some patients, in whom measures of systolic function were initially normal but became abnormal over time, had severe reduction in the E-F slope at the initial examinations and showed gradual decrease. Moreover, the other patients, with normal systolic performances in their last echocardiograms, had more advanced diastolic abnormalities. Thus it appears that diastolic abnormalities gradually progress and that they are already severe before the appearance of impaired systolic function.

At the final examinations, we found marked ventricular hypertrophy in one-fourth of the patients, reduced left ventricular diastolic function in all, and impaired systolic function in three-fourths. Left ventricular internal dimension was decreased in one-fourth and was normal in the remainder. The granular sparkling appearance was newly observed in two patients. Their ventricular wall thickness increased and left ventricular systolic and diastolic function became reduced during the follow-up studies. Subsequently, both showed ventricular hypertrophy and severe abnormalities of systolic as well as diastolic function. However, the cross-sectional studies demonstrated left ventricular diastolic abnormalities in all patients who showed granular sparkling echoes, whereas systolic function was preserved in about a half of them. Their IVST and PWT were found to be slightly greater when compared with those in patients who showed no refractile pattern in the myocardial walls, although some of the other patients had no highly refractile myocardial echo pattern in spite of mild hypertrophy and no other difference in the echocardiographic measurements. We have no explanation for the different myocardial echo pattern among patients who had mild wall hypertrophy, but the above findings show that increased wall thickness, which may be attributed to the more extensive amyloid deposition, is mainly related to the appearance of the granular sparkling echoes, even in the presence of normal systolic function. At the serial studies, it is likely that our follow-up intervals were too long, so that both patients already had systolic abnormalities when highly refractile echoes were visualized. We thus emphasize that, regardless of systolic function, granular sparkling echoes appear after wall hypertrophy with more advanced abnormalities of left ventricular diastolic function develops and that these echoes are obvious with the progression of the amyloid deposition, when ventricular walls are markedly thick-

![Figure 3](http://circ.ahajournals.org/) Serial two-dimensional echocardiograms from the same patient case as in figure 2. A, At the initial examination, both IVST and PWT are normal and highly refractile echoes are not seen in the myocardium. B, At the final examination, the interventricular septum and ventricular wall are thickened. An increased refractile pattern is observed in the interventricular septum. Both the left and right atria are enlarged. L = left; R = right; S = superior; I = inferior.

### Table 6
Serial M mode echocardiographic findings in two patients who had granular sparkling appearance at the final examination

<table>
<thead>
<tr>
<th>Measurements</th>
<th>Patient 2</th>
<th></th>
<th>Patient 5</th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Initial</td>
<td>Final</td>
<td>Initial</td>
<td>Final</td>
</tr>
<tr>
<td>IVST (mm)</td>
<td>9</td>
<td>15</td>
<td>9</td>
<td>17</td>
</tr>
<tr>
<td>PWT (mm)</td>
<td>10</td>
<td>14</td>
<td>10</td>
<td>14</td>
</tr>
<tr>
<td>E-F slope (mm/sec)</td>
<td>52</td>
<td>40</td>
<td>64</td>
<td>54</td>
</tr>
<tr>
<td>DEVM (mm/sec)</td>
<td>73</td>
<td>60</td>
<td>77</td>
<td>64</td>
</tr>
<tr>
<td>%FS</td>
<td>35</td>
<td>28</td>
<td>53</td>
<td>19</td>
</tr>
<tr>
<td>mVcf (m/sec)</td>
<td>1.20</td>
<td>0.88</td>
<td>1.67</td>
<td>0.61</td>
</tr>
</tbody>
</table>
PATHOPHYSIOLOGY AND NATURAL HISTORY—AMYLOIDOSIS

FIGURE 4. Serial M mode echocardiographic measurements during the follow-up studies. Ten patients had one follow-up study and the remaining two had two studies. There occurred significant increases in the IVST and PWT and reductions in the E-F slope of the anterior mitral valve, DEVM of the posterior wall, %FS, mVcf, and left ventricular internal end-diastolic dimension (Dd), without significant change in left ventricular internal end-systolic dimension (Ds). The duration of follow-up (in months) is indicated next to the follow-up values in each panel. Values are mean ± SD. PE = newly developed pericardial effusion; NS = not significant.

ened and severe abnormalities of systolic as well as diastolic function develop. Pericardial effusion and valve thickening were found in some patients whose systolic function was severely impaired.

Although our experience is limited to FAP, we propose, on the basis of the results of this echocardiographic study, that the natural history of amyloid heart disease would pass through the following stages: (1) small amounts of amyloid deposition with focal thickening and resultant reduction in left ventricular compliance; (2) wall hypertrophy caused by more extensive amyloid deposition, more advanced diastolic abnormalities with preserved systolic function, and with some patients showing highly refractile myocardial echoes; (3) very marked thickening of the walls and valves, obvious granular sparkling appearance, pericardial effusion, normal or decreased left ventricular internal dimension, and marked abnormalities of systolic as well as diastolic function. It has been reported by several investigators 8, 17 that some patients with amyloid heart disease had dilated ventricles. Although this finding was absent in our study, presumably some patients who had other conditions such as coronary heart disease and/or chronic lung disease that might cause dilatation would go on to a subsequent stage, a picture of dilated cardiomyopathy, but with thick walls. To establish this hypothesis, further investigations of other forms of amyloid heart disease are necessary.

We are grateful to Shozo Kusama, M.D., Professor of the First Department of Internal Medicine, and Nobuo Yanagisawa, M.D., Professor of the Third Department of Internal Medicine, Shinshu University School of Medicine, for their valuable suggestions and help.

References
4. Chiaramida SA, Goldman MA, Zema MJ, Pizzarelo RA, Gold-
HONGO and IKEDA

9. Andrade C: A peculiar form of peripheral neuropathy: familial atypical generalized amyloidosis with special involvement of the peripheral nerves. Brain 75: 408, 1952
20. Coelho E, Pimentel JC: Cardiac involvement in a peculiar form of paramyloidosis. Am J Cardiol 8: 624, 1961
Echocardiographic assessment of the evolution of amyloid heart disease: a study with familial amyloid polyneuropathy.
M Hongo and S Ikeda

Circulation. 1986;73:249-256
doi: 10.1161/01.CIR.73.2.249

Circulation is published by the American Heart Association, 7272 Greenville Avenue, Dallas, TX 75231
Copyright © 1986 American Heart Association, Inc. All rights reserved.
Print ISSN: 0009-7322. Online ISSN: 1524-4539

The online version of this article, along with updated information and services, is located on the World Wide Web at:
http://circ.ahajournals.org/content/73/2/249