Morphologic Findings in Human Cardiac Allografts

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SUMMARY
Morphologic findings in human cardiac allografts from 13 patients are presented. In the acutely rejected cardiac allograft there was a cellular infiltrate consisting of large lymphocytes and varying numbers of polymorphonuclear leukocytes, eosinophils, and histiocytes in the myocardium and arterial intima. The coronary arteries frequently exhibited degeneration, acidophilia, and vacuolation of the tunica media. In the cases with chronic cardiac allograft rejection there was oblitative fibrous thickening of the arterial intima with medial necrosis. Focal areas of myocardial necrosis and fibrosis were present along with a myocardial infiltrate of mononuclear cells. In most patients who died of causes other than rejection, there was evidence of an immunologic response. Rejection has not been regarded as an “all or none” phenomenon. There was indication in this series that survival was related to histocompatibility.

Additional Indexing Words:
Cardiomyopathy  Acute cardiac allograft rejection  Chronic cardiac allograft rejection
Serratia  Cytomegalic inclusion disease  Cardiac arteriolarsclerosis

DESCRIPTIONS of the gross and microscopic structural changes in allografted cardiac tissue in dogs and humans have been published. The limited number of observations in humans does not permit an analysis of the effect of survival time or the severity and type of tissue response.

The pioneer work of Kosek and co-workers on canine allografts provides the opportunity for comparison with the morphologic response in human cardiac allografts. In many respects the structural alterations of rejection in human and canine cardiac allografts are similar. Further comparison can be made with human renal allografts in which vascular changes similar to those in cardiac allografts have been found.

The primary objective of this paper is to describe the cardiac allograft morphology in 13 patients who survived varying lengths of time following allograft implantation and to compare the observed anatomic changes.

Methods
Fourteen patients received cardiac allografts at St. Luke's Episcopal Hospital during a 10-month period. Clinical data and the surgical technics utilized have been previously reported. The
Table 1

<table>
<thead>
<tr>
<th>Group</th>
<th>Case</th>
<th>Age (yr)</th>
<th>Primary heart disease</th>
<th>(Terasaki) tissue matching grade</th>
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<tbody>
<tr>
<td>Group I</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infection deaths</td>
<td>1</td>
<td>48</td>
<td>Advanced coronary atherosclerosis; old myocardial infarcts; left ventricular aneurysm</td>
<td>C</td>
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<tr>
<td></td>
<td>2</td>
<td>62</td>
<td>Advanced coronary atherosclerosis; old myocardial infarcts; left ventricular aneurysm</td>
<td>C—</td>
</tr>
<tr>
<td>Group II</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Infection deaths</td>
<td>3</td>
<td>55</td>
<td>Advanced coronary atherosclerosis; old myocardial infarcts</td>
<td>C</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>49</td>
<td>Moderate coronary atherosclerosis; cardiac arteriolarsclerosis; multiple areas of myocardial fibrosis</td>
<td>C</td>
</tr>
<tr>
<td></td>
<td>5</td>
<td>50</td>
<td>Advanced coronary atherosclerosis; old myocardial infarcts</td>
<td>C—</td>
</tr>
<tr>
<td>Group III</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(acute cardiac allograft rejection)</td>
<td>6</td>
<td>50</td>
<td>Moderate coronary atherosclerosis; cardiomyopathy</td>
<td>D</td>
</tr>
<tr>
<td></td>
<td>7</td>
<td>54</td>
<td>Advanced coronary atherosclerosis; old myocardial infarcts</td>
<td>D</td>
</tr>
<tr>
<td>Group IV</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>(chronic cardiac allograft rejection)</td>
<td>8</td>
<td>52</td>
<td>Advanced coronary atherosclerosis; old myocardial infarcts</td>
<td>C</td>
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<td>9</td>
<td>54</td>
<td>Advanced coronary atherosclerosis; old myocardial infarcts; left ventricular aneurysm</td>
<td>C—</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>46</td>
<td>Advanced coronary atherosclerosis; old myocardial infarcts; left ventricular aneurysm</td>
<td>D</td>
</tr>
<tr>
<td></td>
<td>11</td>
<td>57</td>
<td>Advanced coronary atherosclerosis; old myocardial infarcts</td>
<td>C</td>
</tr>
<tr>
<td></td>
<td>12</td>
<td>47</td>
<td>Old rheumatic heart disease</td>
<td>C</td>
</tr>
<tr>
<td></td>
<td>13</td>
<td>58</td>
<td>Advanced coronary atherosclerosis; old myocardial infarcts; left ventricular aneurysm</td>
<td>C+</td>
</tr>
<tr>
<td>Surviving patient</td>
<td>14</td>
<td>50</td>
<td>Advanced coronary atherosclerosis; old myocardial infarcts</td>
<td>D</td>
</tr>
</tbody>
</table>

* Second cardiac allograft performed 2 days before patient's demise.
† Survival time to April 19, 1969.
‡ No autopsy performed.

The primary heart disease of each recipient is listed in Table 1.

In all cases, immunosuppressive therapy consisted of corticosteroids, azathioprine (Imuran), and antilymphocyte globulin. Tissue compatibility was estimated by (1) ABO blood group compatibility, (2) lymphocyte crossmatch, and (3) lymphocyte antigen match using Terasaki's microdroplet cytotoxicity technic of grading system A-F. Initial histocompatibility studies were performed preoperatively in Houston and compared with more extensive testing subsequently performed by Terasaki in Los Angeles.

Thirteen of the fourteen patients died at varying intervals following operation, and autopsy was performed on all 13.

The cardiac allografts of all 13 patients were initially examined and the specimens were...
<table>
<thead>
<tr>
<th>Survival days</th>
<th>Clinically recognized episodes of rejection</th>
<th>Cause of death of recipient</th>
<th>Donor</th>
<th>Age (yr)</th>
<th>Sex</th>
<th>Type of brain damage</th>
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</thead>
<tbody>
<tr>
<td>2</td>
<td>0</td>
<td>Pneumonia (Enterobacter-Klebsiella and Escherichia)</td>
<td></td>
<td>15</td>
<td>M</td>
<td>Blunt trauma</td>
</tr>
<tr>
<td>8</td>
<td>0</td>
<td>Pneumonia and septicemia (Pseudomonas)</td>
<td></td>
<td>36</td>
<td>M</td>
<td>Blunt trauma</td>
</tr>
<tr>
<td>47</td>
<td>0</td>
<td>Pneumonia (Serratia)</td>
<td></td>
<td>27</td>
<td>F</td>
<td>Cerebral hemorrhage</td>
</tr>
<tr>
<td>56</td>
<td>1</td>
<td>Septicemia and pneumonia (Serratia); gastrointestinal hemorrhage</td>
<td></td>
<td>40</td>
<td>F</td>
<td>Metastatic melanoma to brain</td>
</tr>
<tr>
<td>68</td>
<td>1</td>
<td>Pneumonia; pulmonary abscesses; septicemia (Pseudomonas)</td>
<td></td>
<td>37</td>
<td>F</td>
<td>Glioblastoma multiforme</td>
</tr>
<tr>
<td>6</td>
<td>1</td>
<td>Acute rejection</td>
<td></td>
<td>15</td>
<td>M</td>
<td>Blunt trauma</td>
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<tr>
<td>13</td>
<td>1</td>
<td>Acute rejection</td>
<td></td>
<td>40</td>
<td>M</td>
<td>Cerebral hemorrhage</td>
</tr>
<tr>
<td>126</td>
<td>3</td>
<td>Chronic rejection</td>
<td></td>
<td>49</td>
<td>F</td>
<td>Cerebral hemorrhage</td>
</tr>
<tr>
<td>146</td>
<td>2</td>
<td>Chronic rejection</td>
<td></td>
<td>17</td>
<td>M</td>
<td>Massive cerebral hemorrhage due to A-V malformation</td>
</tr>
<tr>
<td>149</td>
<td>6</td>
<td>Chronic rejection</td>
<td></td>
<td>50</td>
<td>M</td>
<td>Massive cerebral hemorrhage due to ruptured cerebral aneurysm</td>
</tr>
<tr>
<td>170</td>
<td>3</td>
<td>Chronic rejection; septicemia and meningitis (Listeria monocytogenes)</td>
<td></td>
<td>16</td>
<td>M</td>
<td>Blunt trauma</td>
</tr>
<tr>
<td>204</td>
<td>2</td>
<td>Chronic rejection</td>
<td>(1) 15</td>
<td>F</td>
<td></td>
<td>Bullet wound</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td>(2) 47*</td>
<td>F</td>
<td></td>
<td>Massive intracerebral hemorrhage</td>
</tr>
<tr>
<td>267</td>
<td>0</td>
<td>Chronic rejection</td>
<td></td>
<td>33</td>
<td>F</td>
<td>Cerebral anoxia following cardiac arrest</td>
</tr>
<tr>
<td>164†</td>
<td>3</td>
<td>Living</td>
<td></td>
<td>38</td>
<td>F</td>
<td>Cerebral hemorrhage†</td>
</tr>
</tbody>
</table>

reviewed collectively for this study. Numerous sections were prepared for histologic examination from each specimen. In most cases all of the major extramural coronary arteries were dissected from the heart, fixed in 10% formalin, grossly sectioned, and entirely embedded in paraffin blocks. Sections 7 microns in thickness were prepared from each block. The myocardium was placed in 10% formalin fixative, and in some instances representative portions were fixed in Zenker’s solution. All tissue samples were stained with hematoxylin and eosin and selected sections were examined after special staining with Mallory’s trichrome connective tissue stain, Verhoeff’s elastic stain, methyl green pyronine stain, acid-fuchsin stain, congo red stain, crystal violet stain, and periodic acid-Schiff reaction. Oil red O stains were used for fresh and formalin-fixed frozen sections.

For the convenience of discussion, the patients are divided into four groups, depending on the cause of death and survival time: Group I (cases 1 and 2) consisted of patients expiring in relatively short periods of time after operation (2 and 8 days) due to causes other than cardiac allograft rejection. In group II (cases 3, 4, and 5)
Table 2

Summary of Postmortem Diagnoses Other Than Heart

<table>
<thead>
<tr>
<th>Group</th>
<th>Case</th>
<th>Diagnosis</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>1</td>
<td>Acute bilateral pneumonia due to Enterobacter-Klebsiella and Escherichia.</td>
</tr>
<tr>
<td>Infection deaths</td>
<td>(2-8 day survival)</td>
<td>Chronic passive congestion of liver, spleen, and lungs due to preoperative intractable heart failure. Pulmonary infarction, focal. Small stress ulcers (2) of stomach.</td>
</tr>
<tr>
<td></td>
<td>2</td>
<td>Acute bilateral pneumonia due to Pseudomonas. Pseudomonas septicemia. Pseudomonas ulcers of small and large bowels. Focal recent infarcts of kidneys, spleen, prostate, right testis, and left frontal cerebral lobe due to embolization from left ventricular mural thrombus present in surgically excised heart. Abdominal aortic aneurysm with mural thrombus and early gangrene of distal left leg. Chronic passive congestion of liver, spleen, and lungs. Cardiac cirrhosis. Small stress ulcers (3) of stomach.</td>
</tr>
<tr>
<td>II</td>
<td>3</td>
<td>Acute bilateral pneumonia due to Serratia. Pancreatic necrosis, multifocal.</td>
</tr>
<tr>
<td>Infection deaths</td>
<td>(47-68 day survival)</td>
<td>Septicemia and acute bronchopneumonia due to Serratia. Right inguinal abscess (Serratia cultured). Gastrointestinal hemorrhage due to gastric and duodenal ulcers. Cirrhosis, post-necrotic type. Pancreatic necrosis, multifocal and peripancreatic fat necrosis. Herpes infection of lower face and lips.</td>
</tr>
<tr>
<td></td>
<td>4</td>
<td>Acute pneumonia and multiple pulmonary abscesses of right lung due to Pseudomonas. Cytomegalic inclusion disease involving lungs and pancreas. Herpes infection involving face and buccal mucosa. Prostatic adenocarcinoma, invasive.</td>
</tr>
<tr>
<td>III</td>
<td>5</td>
<td>Interstitial pulmonary fibrosis and hemosiderin deposition (brown induration of lungs).</td>
</tr>
<tr>
<td>(Chronic cardiac allograft rejection)</td>
<td>9</td>
<td>Chronic passive congestion of liver, spleen, and lungs. Pleural effusion. Pancreatic necrosis, multifocal.</td>
</tr>
<tr>
<td></td>
<td>10</td>
<td>Chronic passive congestion of lungs. Pleural effusion. Pancreatic necrosis, multifocal.</td>
</tr>
<tr>
<td></td>
<td>13</td>
<td>Passive congestion of liver and lungs. Pancreatic necrosis, multifocal.</td>
</tr>
</tbody>
</table>

were the patients expiring between 47 and 68 days after operation from causes other than cardiac allograft rejection.

In group III (cases 6 and 7) were the patients expiring on the sixth and the 13th day after operation who had clinical7 and morphologic evidence of acute cardiac allograft rejection.

In group IV (cases 8 through 13) were the patients expiring between 126 and 267 days after operation who had clinical7 and morphologic evidence of chronic cardiac allograft rejection.

Autopsy summaries are given in table 2.

Results

Group I

The cardiac allograft from each case appeared grossly uncomplicated. The hearts of cases 1 and 2 weighed 430 and 390 g, respectively.

Microscopically, there was interstitial edema of the myocardium with wide separation of the myocardial fibers. Many lymphatic vessels of the myocardium were dilated, a
finding attributed to severance of the heart lymphatics. The extramural and mural coronary arteries were unremarkable with the exception of the endothelial cells, which were sometimes enlarged. Rarely, an aggregate of mononuclear cells consisting primarily of large lymphocytes was found in the interstitium (fig. 1) and the adventitia of myocardial vessels.

**Group II**

The cardiac allografts in cases 3, 4, and 5 weighed 410, 385, and 400 g, respectively. The pericardium was focally adherent to the epicardium due to fibrous adhesions. The surgical suture lines between donor and recipient myocardia were healing well. No thrombi were found. In case 4 there was a small (0.7 cm) endocardial hemorrhagic focus involving the posterior papillary muscle of the mitral valve. In case 5 multiple hemorrhages were seen in the allografted portion of the right atrial endocardium.

Dilatation of the cardiac chambers was not present in these three cases, and there was no thickening of the atrial or ventricular walls. The myocardium appeared normal on gross examination. The tricuspid, pulmonary, mitral, and aortic valves were grossly and microscopically normal. Microscopically, abnormal fibrous connective tissue produced a diffuse uniform thickening of the tunica intima of the coronary arteries. There was no associated mononuclear infiltrate, and medial necrosis of the arteries was not evident. The internal

**Figure 1**

Cardiac allograft at 8 days (case 2). Rare aggregates of mononuclear cells with extravasated erythrocytes in myocardium. Most mononuclear cells are plump lymphocytes. Foci such as this were rare in this specimen, but were felt to represent an immunologic response. Reduced from $\times 850$. 
Cardiac allograft at 56 days (case 4). Section reveals dilatation of lymphatic vessels. Reduced from × 425.

Figure 2

elastie membrane was intact. (The intimal thickening found in each of these allografts was probably due to the status of the vessels at the time of transplantation, but an immunologic reaction could have conceivably contributed to the fibrous intimal thickening.)

In the group II cases interstitial edema and lymphatic dilatation (fig. 2) were present but were not as generalized as in group I, presum-

Figure 3

Acute rejection (case 6). Heart at 6 days showing right atrium and ventricle. Recipient and donor portions of right atrium are strikingly different, and surgical suture (arrow) represents line of demarcation in the appearance. Endocardium of donor atrium and ventricle is markedly hemorrhagic. There is thickening of the ventricular walls. The myocardium is mottled and darkened.

Circulation, Volume XLI, March 1970
Acute rejection (case 7). Patient survived 13 days. Microscopic cellular infiltrate, which was diffuse and dense, consisted of lymphocytes, histiocytes, scattered polymorphonuclear leukocytes, and eosinophils. The infiltrate was more pronounced in perivascular areas. Fibrin deposition was sometimes associated with the cellular infiltrate. Arrows point to polymorphonuclear leukocytes. Reduced from × 850.

ably due to reanastomoses of lymphatic vessels. Myocytolysis identified by clearing of sarcoplasm and sometimes swelling of the myocardial fibers was found in some areas, but this was not a pronounced feature. Interstitial aggregates of mononuclear cells, consisting of lymphocytes and plasma cells, were found infrequently. Some of the lymphocytes were selectively stained by methyl green pyronine. Some groups of myocardial fibers exhibited fuchsinophilia consistent with myocardial fiber damage. Fuchsinophilia was especially pronounced in myocardial fibers subjacent to areas of myocytolysis.

Group III

The cardiac allografts in cases 6 and 7 weighed 535 and 430 g, respectively. The epicardial surface of each was dull, dark red, mottled, and covered with fibrin. The myocardium was firm, dark reddish brown, and mottled. There was obvious thickening of the right and left ventricular walls (measuring 1.3 and 2.2 cm, respectively). The cardiac chambers were not notably dilated. Large areas of hemorrhage were seen on all the endocardial surfaces of the allografted heart chambers. There was sharp demarcation at the atrial suture lines, and the endocardial hemorrhagic foci were not present in the recipient portions of the atria (fig. 3).

Microscopically, separation and narrowing of myocardial fibers by interstitial edema and
infiltration of mononuclear cells and varying numbers of polymorphonuclear leukocytes were apparent (fig. 4). The predominant mononuclear cell was a large lymphocyte with a large vesicular to hyperchromatic nucleus which occupied most of the cell, leaving only a thin rim of cytoplasm. Histiocytes in varying numbers were admixed with the other mononuclear cells. Erythrocytes were extravasated into the interstitium in scattered areas. Occasionally, eosinophils were identified. The cellular infiltrate, which was heavy and diffuse throughout the allograft myocardium but especially so in perivascular areas, also contained some eosinophils. Some myocardial fibers had separated and fragmented. In these areas there was accumulation of mononuclear cells, polymorphonuclear leukocytes, and fibrin. In general, cross striations of myocardial fibers were preserved. Lymphatic vessels were dilated and there was capillary congestion. Capillary rupture was held responsible for the extravasated erythrocytes. The extramural and intramural coronary arteries were abnormal; the intact endothelial cells were enlarged, and there were multiple areas of disruption of the endothelial layer. The intima was thickened, vacuolated, and loosely arranged. A cellular infiltrate, similar to that found within the myocardium, was present in the intima and within the adventitia. Some small intramural arteries exhibited degeneration, vacuolation, and acidophilia of the tunica media (fig. 5). The tunica media of the major extramural

Figure 5
Acute rejection (case 7). Same specimen as figure 4. Intramural arteriole. There is degeneration of the tunica media. Enlarged endothelial cells are present. Tunica media exhibits vacuolation and acidophilia. Mononuclear cellular infiltrate is present in the adventitia. Reduced from \( \times \) 425.
coronary arteries was necrotic in some areas but normal in others. There was no interstitial cellular infiltrate or vascular change in the recipient portions of the right and left atria.

In the atroventricular valves a subendothelial cellular infiltrate similar to that observed in the myocardium was found.

Viral cultures of the myocardium from each allograft were negative.

**Group IV**

The weight of the cardiac allografts at necropsy of cases 8 through 13 was 445, 460, 510, 450, 362, and 456 g, respectively. The anastomotic lines between donor and recipient portions were uncomplicated. The epicardial surfaces of all hearts appeared dull. Adherence of the pericardia to the epicardia was due to the presence of fibrous adhesions. Some myocardia were flabby while others were firm. In individual cases the myocardium was of uniform appearance, but there were gross differences in myocardial appearance between cases. The myocardium in case 12 was brownish tan, pale, and exhibited no gross evidence of necrosis. The myocardia of the other five specimens were grossly mottled. The endocardia of the allografts were hemorrhagic, except in cases 12 and 13. The cusps of the tricuspid, pulmonary, mitral, and aortic valves were grossly normal. The lumina of the major coronary arteries and their extramural
branches were grossly compromised, and intimal fibrofatty streaks were found. No thrombi were found in the chambers or vessels of the allografts.

Microscopically, there was considerable variation from one case to another, but certain patterns of response could be recognized. In the major coronary arteries fibrous intimal thickening and proliferation with varying degrees of luminal obliteration were present (figs. 6 to 8). The intimal thickening was often not uniform in an individual vessel, and the narrowed lumen was often eccentric in position and irregular in shape. The central portions of the intima were often more loosely arranged and less compact than the peripheral portions (figs. 6 and 7). No increase in elastic fibers was evident in the subendothelial connective tissue. Intact endothelial cells often appeared enlarged. Small fibrin thrombi attached to the arterial intima were rarely encountered. The thickened intima contained an infiltrate of mononuclear cells consisting of lymphocytes, pyroninophilic mononuclear cells, and histologically mature plasma cells. Histiocytes were present in varying numbers within the intima (fig. 9), and cytoplasmic lipid vacuoles (oil red O positive substance) were frequently demonstrated in the histiocytes. Extracellular fat globules were also demonstrated in the intima as well as within the tunica media. The

Circulation, Volume XLI, March 1970
Chronic rejection (case 13). Extramural branch of coronary artery. Patient expired 267 days following surgery. There is pronounced fibrous intimal proliferation with luminal compromise. Mononuclear infiltrate is found in all vessel layers. Medial necrosis is present. Hematoxylin and eosin; reduced from ×82.

Internal elastic membrane was more prominent than usual in the hematoxylin and eosin sections and was frequently crenulated. Areas of fragmentation and absence of the internal elastic membrane were revealed by elastic stains. Necrosis of the tunica media was found in the extramural and intramural coronary arteries (fig. 10). Microaneurysms were rarely found (fig. 11). Partial fibrous tissue replacement of the tunica media was evident in some arteries. No amyloid deposits could be demonstrated in the vessel wall by amyloid stains (congo red and crystal violet with and without polarization). Intramural and extramural veins were normal except for focal adventitial infiltrate of mononuclear cells.

Myocardial fibers were separated and narrowed, presumably due to interstitial edema. Patchy areas of myocardial cell damage were evident by focal acidophilia in the hematoxylin and eosin stain (fig. 12) and by focal fuchsinophilia when using acid fuchsin stain. Myocytolysis was seen in many areas. The swollen and clear myocardial fibers contained brownish tan granular particles of lipofuchsin pigment (fig. 13). Microscopic areas of

Figure 8

Chronic rejection (case 13). Extramural branch of coronary artery. Patient expired 267 days following surgery. There is pronounced fibrous intimal proliferation with luminal compromise. Mononuclear infiltrate is found in all vessel layers. Medial necrosis is present. Hematoxylin and eosin; reduced from ×82.
interstitial fibrosis were found that contained a mononuclear cell infiltrate and appeared to be healing areas of myocytolysis. An interstitial infiltrate of mononuclear cells (large and small lymphocytes, pyroninophilic mononuclear cells, and histologically mature plasma cells) was seen; the quantity of the infiltrate varied from case to case. Polymorphonuclear leukocytes were present but were relatively rare. Mononuclear infiltration was often dense in the endocardium and subendocardium of the allograft. In cases 8 and 13 small microscopic inflammatory infiltrates were seen in the subendothelial tissue at the base of the tricuspid and mitral valves. The valves were otherwise normal. Interstitial extravasation of erythrocytes was present. In case 9 and 12 (two of the longer survivors) calcification of individual myocardial fibers was seen. Autonomic nerve fibers and ganglia were present

Figure 9

Chronic rejection (case 12). Same specimen as in figure 7. High magnification of intramural coronary arterial intima in cardiac allograft at 202 days. There are aggregates of lipid-laden histiocytes (H). Oil red O stains revealed the lipid to be intracellular and extracellular, and also present in the tunica media. Internal elastic membrane (IM) is apparent. Endothelial cells (E) are intact in this section. Lymphocytes and occasional plasma cells are found within the intima. Donor was a 15-year-old girl. Hematoxylin and eosin; reduced from × 825.
and surrounded by a perineural mononuclear infiltrate. The Schwann cells were intact and exhibited good alignment.

The epicardia were thickened, fibrotic, edematous, and contained a mononuclear infiltration which was out of proportion to that generally observed in the postpericardiotomy state.

Viruses could not be cultured from the allografts of cases 8 through 12.

Discussion

The mean survival time of groups I and II was 36 days and in each case infection was primarily responsible for the death of the patients. The two patients who expired from acute cardiac allograft rejection (group III) had a mean survival time of 10 days. The mean survival time for patients with chronic cardiac allograft rejection (group IV) was 177 days.

Although morphologic changes in the allografts in patients dying from rejection are variable from one case to another, certain histologic patterns are observed which are regarded as host-allograft reaction. The reac-
Figure 11

Chronic rejection (case 9). Same specimen and vessel as figure 10. Fibrous intimal proliferation with mononuclear infiltrate. Microaneurysm present at focus of medial necrosis. Hematoxylin and eosin; reduced from × 115.

tion has not been found to be an all or none phenomenon. In patients dying of causes other than allograft rejection (groups I and II), there was evidence of an immunologic response, but the reactions in the cardiac allograft were not of a magnitude sufficient to contribute to the patient's death. In group I a rare aggregate of mononuclear cells consisting principally of large lymphocytes was found. In group II there were focal myocytolysis, focal fuchsinophilia, and rare aggregates of mononuclear cells, but these morphologic traits were quantitatively less than those observed in groups III and IV in which the morphologic changes were profound. In chronic rejection the obliterator vascular lesions reduce blood flow. However, the lumen is probably greater in size under physiologic pressures during life than when observed in the conventional histologic sections.

All the donors in the series had intracranial damage. Focal areas of myocardial damage and edema may occur in patients dying from intracranial lesions. Some of the lesions observed in the cardiac allograft may conceivably be secondary to the status of the heart at
Figure 12

Chronic rejection (case 9). Myocardium of cardiac allograft at 146 days. There is variance in the tinctorial qualities of the sarcoplasm. Extravasation of the erythrocytes is present. Note nucleus (arrow) exhibiting karyorrhexis. Myocardial fibers are separated. Hematoxylin and eosin; reduced from ×850.

the time of transplantation, especially those of patients with relatively short survival after surgery.

Eight of the 13 patients had small areas of pancreatic necrosis demonstrated at autopsy and attributed to corticosteroid therapy.15, 16

Correlation between the Terasaki histocompatibility grade with the length and quality of survival of the recipients was apparent in this small series. A decrease in both mean survival time and survival time without a clinical recognized episode of rejection has been observed with decrease in histocompatibility grade from C+ to D (fig. 14 and table 1). A corollary observation has been made that the number of rejection episodes increases with decreasing grade of histocompatibility from no clinically detected episodes per 250 patient days in the C+ matches to one episode of rejection per 26 patient days in the grade D matches.

Acknowledgment

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Figure 13

Chronic rejection (case 10). Myocardial fibers exhibiting myocytolysis. Arrow points to aggregate of lipofuscin pigment. Hematoxylin and eosin; reduced from × 850.
HUMAN CARDIAC ALLOGRAFTS

Survival According to Histocompatibility

Survival according to histocompatibility.

autopsy information and material in case 13, and to Dr. Gustave J. Dammin, Boston, Massachusetts for his comments concerning cases 6, 9, 12, and 13.

References


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