The Relationship of Aging to Histological Changes in the Conduction System of the Normal Human Heart

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Summary

The effect of aging on histological changes of the conduction system was studied by serially sectioning 55 autopsied hearts weighing less than 300 Gm. None of the hearts showed evidence of cardiovascular disease nor were there any abnormalities in the clinical findings and ECG taken during the last 3 months of life. A reduction in the number of muscle cells and an increase in the number of collagen fibers were apparent in hearts taken from patients over 70 years of age. These findings were most evident in the S-A node and less so in A-V node, bundle of His, and left and right bundle branches. Deposition of amyloid substances was not observed in any portion of the conduction system.

Additional Indexing Words:
Cardiac conduction system Histology Geriatric alterations Amyloid substance

There has been much interest in the correlation between anatomic lesions and physiologic events of the cardiac conduction system in pathological conditions.1–3) One of us (M. F.) studied such a correlation in Kimmelstiel-Wilson syndrome,14) cardiac amyloidosis15) and left bundle branch block,16) and found common features related to aging of the conduction system. However, there have been only a few histological studies,4–7) and almost none in Japan.

This study reports on histological data on aging of the conduction system in hearts without organic heart disease obtained at autopsy. The findings are compared with the data of other workers. Amyloid deposition was also carefully investigated since previous studies on senile cardiac amyloidosis...
have revealed discrepancies.\textsuperscript{13),15),17}-19)

\textbf{MATERIALS AND METHODS}

Fifty-five hearts were obtained from autopsied patients who had no clinical sign of cardiovascular disease nor abnormalities on ECGs taken during the last 3 months of life. Most of these patients died of neoplasms. Table I shows the age and sex distribution of the patients. All hearts weighed less than 300 Gm. Macroscopic examination of the coronary arteries showed stenotic lesions occluding no more than 25\% of the lumen.

The sino-atrial (S-A) node and its approach, atrio-ventricular (A-V) node, bundle of His, and both bundle branches were serially sectioned and every 10th section was stained according to the method of Lev.\textsuperscript{8),9) Alternate sections were stained with hematoxylin-eosin, Weigert-van Gieson, and Congo red. Amyloid deposition was detected by the characteristic green-yellow coloration seen on polarizing microscopy following Congo red staining. The ratio of collagen to muscle cells in the S-A node, A-V node, bundle of His, and both bundle branches was calculated semi-quantitatively.

\textbf{RESULTS}

In the S-A nodes, of patients over 70 years of age, the number of muscle cells was smaller and the number of collagen fibers was larger as compared to the S-A nodes of patients aged 60. These differences became more prom-
Fig. 1. Percents of muscle and collagen in S-A node with aging. After 70 years of age, the number of muscle cells decreased while the number of collagen fibers increased.

Fig. 2. S-A node of a 24-year-old man (left) and a 67-year-old man (right). N=S-A node; F=fat. (Weigert-van Gieson stain ×12)

In the adjacent atrial muscle and subepicardial space, there was more fat tissue in older patients.

inent with increasing age, as shown in Fig. 1. Adipose tissue within the node did not increase with age. Typical findings of the S-A node and its approach are shown in Fig. 2. There was no difference in the size of the S-A node, but in the adjacent atrial muscle and subepicardial space, there was more adipose tissue in nodes taken from the older patients. A high magnification of the S-A node revealed more abundant muscle cells in the tissue from younger (Fig. 3, left), as compared with older patients (Fig. 3, right), whereas collagen fibers and elastic fibers were more abundant in tissues from older patients.

There were some reductions in the number of conduction cells, in the
Fig. 3. A higher magnification of the S-A node. Increase in the number of collagen fibers with aging (right). M=muscle cells; C=collagen fibers. (Weigert-van Gieson stain ×100)

Muscle cells were more abundant in tissues from younger patients (left) as compared to older patients (right). Muscle cells were rich (left) and more collagen fibers were seen (right).

Fig. 4. Percents of muscle and collagen in A-V node, bundle of His, LBB, and RBB. The A-V node in those over 70 years, bundle of His in those over 40 and left bundle branch in those over 50 showed some reduction in the number of conducting cells, but there was no significant increase in the number of collagen fibers.
A-V node in those over 70 years, bundle of His in those over 40, left bundle branch in those over 70, and the right bundle branch in those over 50, but there was no significant increase in the number of collagen fibers (Fig. 4).

The volume of the muscle cells in the A-V node was smaller in tissues from older patients, as shown in Fig. 5.

Fig. 5. A-V node of a 31-year-old man (left) and a 74-year-old man (right). N=A-V node. (Weigert-van Gieson stain ×12)

Fig. 6. Bundle of His in a 8-year-old boy (left) and a 72-year-old man (right). MB=main bundle. (Weigert-van Gieson stain ×12)
Findings in the bundle of His and the left bundle branch are shown in Figs. 6 and 7, respectively. There were some changes with aging in the left bundle branch but they were less remarkable than in the S-A node.

In contrast to a slight deposition in the contractile and connective tissue of the aged heart, amyloid deposition was not detected in the conduction system.

**DISCUSSION**

Lev et al\(^4\),\(^5\) reported that with advancing age, the increase in collagen fibers of the S-A node was rapid up to the age of 40 and slow thereafter. The amount of elastic tissue also increased up to the age of 50 to 60 years and the reticular fibers also increased, both in number and coarseness, after the age of 40 with apparent loss of muscle fibers. Davies and associates\(^6\),\(^7\) found a significant fall in the number of muscle cells in the S-A and internodal tracts in subjects over 75 years compared with those under 50 years.

The changes we noted were in tissues from patients over 70 years of age. This indicates a somewhat later onset of changes than reported by others. This may be due to the less advanced degree of subclinical coronary atherosclerosis seen in the Japanese. The decreases in the number of muscle cells and increases in the number of collagen fibers were most remarkable in the
S-A node as compared with the other parts of the conduction system.

We found no fatty infiltration in the S-A node with aging, although Lev et al\textsuperscript{10} considered fatty infiltration in and around the S-A node as a part of the aging process. Balsaver\textsuperscript{11} reported that adipose tissue within the sinus node could, by mechanical interference, produce conduction defects. Bronzini and Novi\textsuperscript{12} who studied the atrio-ventricular conduction system in 11 fatty hearts and 15 non-fatty hearts noted infiltration of fatty tissue into the A-V bundle and A-V node only in the fatty hearts.

Amyloidosis has been classified as primary and secondary according to its pathogenesis, though there is a considerable overlap. In primary amyloidosis, there is deposition of amyloid substance in the S-A node, A-V node, and bundle of His.\textsuperscript{15,17,18} Lee and Kaufmann,\textsuperscript{19} Buerger and Braunstein,\textsuperscript{20} Schwartz,\textsuperscript{21} and Pomerance\textsuperscript{22} detected cardiac amyloidosis in the aged. Senile cardiac amyloidosis has been frequently detected in aged persons with the amyloid deposition localized primarily in the myocardial interstitium of the atrial septum under the endocardium.\textsuperscript{13} On the contrary, Davies\textsuperscript{7} and Sugiura\textsuperscript{23} found no deposition of amyloid in the conduction system of the aged. We also found no amyloid substances in the conduction system. The reason for this may be that in our study, the materials were carefully selected, in that all the normal hearts used were from patients under 80 years of age, the hearts weighed less than 300 Gm, ECG data were normal, and there was no organic heart disease.

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### References