SUMMARY The conduction system of the heart was carefully examined at necropsy in two cases of rheumatoid arthritis and one of ankylosing spondylitis. All three patients had cardiac electrical instability and two of the three died suddenly. The electrophysiological abnormalities of the three patients included paroxysmal atrial fibrillation in the first case, sustained atrial fibrillation with complete heart block and escape atrioventricular (A-V) junctional rhythm in the second case, and progressively increasing heart block eventually became complete in the third case. The sinus node exhibited extensive focal degeneration with and without associated inflammation in all three hearts, but the sinus node artery was not remarkably abnormal in any of these. All three hearts had important focal degenerative disease in the A-V node and His bundle, and in each of these there was marked narrowing of the local nutrient arteries, amounting to virtual occlusion in two hearts. The probable relationship of these postmortem histological findings to the electrocardiographic disturbances in each patient is discussed. Abnormalities in the cardiac conduction system of the hearts of these three patients are compared to ones previously reported for disseminated lupus erythematosus, polyarteritis nodosa, and scleroderma heart disease.

 THERE ARE SO MANY WAYS in which rheumatoid arthritis involves the heart that the value of their fuller understanding transcends relevance to rheumatology alone. Pericarditis, valvulitis, coronary arteritis, and heart block are among the more familiar manifestations of rheumatoid heart disease, but additional complications include myocardial infarction due to the vasculitis and focal fibrosis and degeneration in all parts of the heart, a special one being the cardiac conduction system. Although their clinical expression is seldom subtle and usually is unmistakable, the initial appearance of almost any feature of rheumatoid heart disease is characteristically late in the clinical course of the arthritis. Furthermore, electrophysiological problems such as heart block typically develop slowly in patients with rheumatoid heart disease and are thus more amenable to optimal treatment. Despite the rather delayed onset of cardiac complications, and their usually slow progression, death from rheumatoid heart disease is often sudden even though seldom unexpected.

A number of excellent reviews are available on the subject of rheumatoid heart disease.1-14 In addition there have been several meticulous postmortem studies of the cardiac conduction system in the hearts of patients who died with heart block or other electrophysiological disturbances.15-21 Perhaps because heart block is the most often recognized electrical disturbance in rheumatoid heart disease, most examinations of the cardiac conduction system have been limited to the A-V (atrioventricular) node and His bundle with their immediate environs, and only two clinicopathological studies20,21 have even mentioned the sinus node. The present report will present clinical findings with postmortem correlation in three patients who had rheumatoid arthritis complicated by disturbances in their cardiac rhythm or conduction. Two of the three died suddenly.

Case Reports

Case 1

A salesman first complained of rheumatism at the age of 32. Recurring discomfort in the wrists and elbows was managed with mild analgesics until the age of 61. By that time he had developed moderate degrees of deformity from rheumatoid arthritis which was initially treated with salicylates and paraffin baths, but later required the additional administration of gold salts. During his sixty-fifth year his rheumatoid arthritis became worse despite treatment and he also developed an inguinal hernia which required surgical repair. Histological examination of the hernia specimen revealed arteritis in multiple sections of the skeletal muscle included. In that same year he began to experience angina pectoris for several months, culminating in an acute myocardial infarction for which he was admitted to the hospital. On admission he had atrial fibrillation with rapid ventricular response (fig. 1), and also had symptoms and findings of congestive heart failure. Treatment with digitalis slowed the heart and his clinical improvement coincided with the restoration of sinus rhythm at a rate of about 100/min. He appeared in good spirits and in satisfactory general condition that evening, when he suddenly died with no preceding complaint or visible change in his condition.

At necropsy examination there was bilateral pleural effusion and other findings attributable to the recent cardiac failure. Marked atherosclerosis was present in the entire coronary circulation, with recent thrombotic occlusion in the proximal third of the left anterior descending coronary artery. Both old and new myocardial infarction was present in the anteroseptal region of the left ventricle. The regions of the sinus node and of the A-V node and His bundle were removed as two separate blocks and studied by subserial section. Except for the coronary disease and myocardial infarction...
tion, gross examination of the heart was normal; there was specifically no valvulitis or pericarditis.

Both the sinus node artery and A-V node artery originated from the right coronary which was narrowed but patent. Focal degeneration was present in and about the sinus node (fig. 2), but its nutrient circulation appeared essentially intact. By contrast, the principal artery to the A-V node was completely occluded by fibromuscular dysplasia (fig. 3). Several of its branches were involved to a lesser degree. There was commensurate focal degeneration within both the

Figure 2. Fatty scars and degeneration, particularly at the junction of sinus node and right atrium of case 1. All the area boxed in A is sinus node and is illustrated at higher magnification in B.

Figure 3. The A-V node artery of case 1 shown here is occluded by focal fibromuscular dysplasia. The section in A is from the posterior margin of the A-V node and the artery (enlarged photomicrograph in B) is indicated with an arrow. There is scarring in the interventricular septum (IVS).
A-V node and His bundle (figs. 4 and 5). There were small areas of inflammation in some sections of the major coronary arteries, but no more than often observed with coronary atherosclerosis.

Case 2

A widow with ten children was first seen in the hospital at the age of 63 complaining of arthritis. The knees, wrists, and hands were swollen, exhibiting typical deformities of rheumatoid arthritis. She was also found to have murmurs of aortic stenosis and insufficiency. Her electrocardiogram at that time and on all subsequent examinations demonstrated atrial fibrillation with a high grade A-V block and an escape A-V nodal rhythm which occasionally varied in regularity, presumably due to interference by occasional resumption of A-V conduction (fig. 6). Some cardiac failure which was present responded well to treatment, as did the rheumatoid arthritis. Two years later she suddenly developed right hemiparesis, the cause of which was undetermined; diagnosis either of a small cerebral embolus or of a transient Stokes-Adams seizure with thrombosis appeared equally likely. During the next year, she made a satisfactory recovery from the stroke except for increasing episodes of drowsiness and
dizziness. Her cardiac rhythm and conduction remained the same as on the initial examination. At the age of 67 she was reported to have suddenly died at a nursing home, and the body was brought to the hospital for postmortem examination.

At necropsy the pertinent findings for this report were in the heart. The brain was not examined. The entire heart was enlarged, weighing 800 grams, with the left ventricle measuring 15 mm and the right 10 mm in thickness. The major coronary arteries were sclerotic but widely patent. The sinus node artery arose from the left circumflex and the A-V node branch from the right coronary artery. Dense adhesive pericarditis covered the entire heart. Both the mitral and tricuspid valves were slightly thickened. The aortic valve was densely calcified, particularly at its free edges and much less near the aorta. The regions of the sinus node and A-V junction were removed and studied with subserial sections.

Focal leukocytic infiltrates of the thickened pericardium included the region over the sinus node. The sinus node was extensively degenerated with fatty and collagenous replacement (figs. 7 and 8). There was a special cystic degeneration of the normal collagen framework of the sinus node (fig. 8A). The arteries of the sinus node region were not remarkable. In the antrum atrii dextri there were both old and recent mural thrombi (fig. 8), which is good evidence of chronically active degeneration of the sinus node and adjacent region.29 Throughout much of the atrium there was focal degeneration and fatty replacement, including large portions of the internodal pathways (fig. 9). Near the aortic valve the central fibrous body contained a large calcific mass. This calcific mass encroached on portions of the His bundle which, along with the A-V node, exhibited focal inflammation and degeneration (fig. 10). Just beneath the origin and the proximal few millimeters of the right coronary artery a second calcific mass protruded through the arterial wall and had disrupted the endothelium, where small aggregates of platelets were present (fig. 11).

Case 3

A business executive who first began having symptoms of rheumatoid arthritis in his twenties was subsequently examined at a number of major medical institutions and was first told that he had ankylosing spondylitis at the age of 35 years. Subsequently he was troubled with polyarthritis particularly involving the lumbar spine, sacroiliac joints, and the knees. There was a biologically false positive serologic test for syphilis. A murmur of aortic insufficiency was present at the first and all subsequent examinations. Over the next
decade his arthritis gradually worsened, as did his cardiac status. The left ventricle progressively enlarged and gradually failed despite treatment. Concomitant with this there was progressive deterioration of A-V conduction over a period of three years, beginning with P-R interval prolongation in the ECG, followed over several months by intermittent bouts of Wenckebach phenomenon and eventually ending in permanent complete A-V block the last two years of life (figs. 12 and 13). His terminal admission was for continual dyspnea refractory to therapy. He died at the age of 47 years due to intractable congestive heart failure.

Necropsy findings of special relevance to this report were those in the heart, which was enormous, weighing over 1000 grams due primarily to the large left ventricle. There was about 80% narrowing of the proximal third of the left anterior descending coronary artery but no other significant lesions in the major proximal coronary trunks. The A-V node artery was provided by the right coronary and the sinus node branch came from the left circumflex. The pulmonic, tricuspid, and mitral valves were normal. The aortic valve commissures were slightly separated (less than 1 mm), but the free edges of all three valve cusps were smoothly thickened and retracted from the center of the valve orifice. Within the left coronary cusp there was a smooth fenestration about 2 mm in diameter; it had no irregularities or encrustations. Except for some thick calcium plaques, the wall of the aorta near the valves was unremarkable. The regions of the sinus node and the A-V junctional tissues were removed for sub-servial sectioning and examination.

There was scattered fibrosis and degeneration in the sinus node and its environs (fig. 14) but the sinus node artery appeared normal. A number of small ventricular arteries were narrowed and some were associated with periarterial inflammation in the left ventricular myocardium, but these were infrequent and most of the ventricular myocardium and its blood supply appeared remarkably good. Both the A-V node and His bundle were essentially destroyed by extensive focal inflammation and degeneration, coupled with widespread obliteration of the local nutrient arteries (figs. 15-18).

Discussion

Damage in the cardiac conduction system of patients with rheumatoid arthritis or ankylosing spondylitis is in part the consequence of narrowing disease in their nutrient arteries, but it is more than that. Pericarditis in case 2 also affected the sinus node, but in both case 1 and case 2 there was more degeneration in the sinus node than could be accounted for on the basis of either a vascular lesion or pericarditis. In all
three cases the focal degenerative lesions in the A-V node and His bundle could only partially be explained by narrowing of their nutrient arteries; for example, in case 3 the focal inflammatory lesions of the A-V node were even more prominent than the arterial lesions. Since the sinus node is normally organized within a collagen framework and the A-V node and His bundle are either bordered directly or completely surrounded by collagen, one is naturally tempted to relate this anatomical feature (proximity to collagen) to the observed degenerative changes.

Within the sinus node of case 2 in particular there was extensive degeneration of the sinus node and its collagen frame, and numerous old and recent thrombi in the directly subjacent antrum atrii dextri, but no significant lesions either in the sinus node or its parent main coronary trunk. Throughout several years of clinical observation of that patient there was never evidence of sinus rhythm, the sustained atrial fibrillation being attributable at least in part to virtually total destruction of the sinus node. It is not so surprising that she eventually had probable Stokes-Adams attacks and died suddenly as it is that her A-V junctional rhythm functioned with reasonable stability for a remarkably long period. The erosive endothelial lesion in the proximal portion of the right coronary artery may have been the source of platelet or other emboli either into the distal coronary branches (although none could be found) or back into the aorta and thence to the systemic circulation, but this is conjectural.

In case 1 there was important coexisting disease in the form of coronary occlusion and myocardial infarction. Although myocardial infarction as a direct consequence of rheumatoid heart disease has been reported,7 the evidence in case 1 did not support that likelihood; rather, this appeared to be coincidental coronary disease in a subject with rheumatoid arthritis. However, the lesion completely occluding the A-V node artery of case 1 is characteristic of those found in rheumatoid heart disease,10,17,18,19,20,21 although similar focal fibromuscular dysplasia of the A-V node artery can also oc-

![Figure 11](image-url)  
**Figure 11.** Another calcific mass within the central fibrous body of case 2 eroded through the wall of the right coronary artery, as shown in A, where an asterisk marks the defect in the endothelium around which there were aggregates of platelets loosely organized. The other margin of the calcific mass with adjacent degeneration of His bundle is illustrated in B.

![Figure 12](image-url)  
**Figure 12.** Earlier in his clinical course the patient in case 3 exhibited varying degrees of incomplete A-V block. A long P-R interval with echo beats is shown in lead I; Wenckebach periods in lead II and stable 2:1 A-V block in lead III; all were recorded in one examination (matter of several minutes).

![Figure 13](image-url)  
**Figure 13.** Later in his clinical course (case 3) there was stable complete A-V block.
FIGURE 14. Both the anterior internodal pathway (AIP in A) and the sinus node (SN in B) of case 3 showed fatty scars and degeneration, although the lumen of the sinus node artery was patent.

cur in the absence of rheumatoid arthritis.\textsuperscript{29} Combined with the other effects of his recent myocardial infarction, the occluded A-V node artery in case 1 may well have contributed to the sudden nature of his death.

The third case is representative of histopathological changes described by others\textsuperscript{9, 15, 16, 18} in the cardiac conduction system of patients with ankylosing spondylitis. There is now evidence that ankylosing spondylitis differs in a number of respects from most forms of rheumatoid arthritis\textsuperscript{6, 24-28} and some challenge the propriety of considering them as forms of the same disease. However, at least as concerns the abnormalities in the region of the A-V node and His bundle, the processes are remarkably similar: multiple narrowings of local nutrient arteries, plus disproportionate focal inflammation and degeneration beyond that attributable to the vascular lesions alone.

Given the extensive appearance of destruction within the A-V node and His bundle of these three hearts, which resemble most examples reported by others,\textsuperscript{15-21} it is surprising that more patients with rheumatoid arthritis do not have failure of A-V conduction earlier in their disease. Syncopal attacks or Stokes-Adams seizures are rarely seen early in the course of rheumatoid arthritis, and even when they appear, the first episodes have seldom been reported as the fatal ones. There are two plausible explanations for this: either the process is remarkably gradual and does not appear in its final form for many years, or it does not begin at all until late and what is seen at necropsy has been rather rapidly progressive. The question is not susceptible to further explanation on the basis of postmortem studies, since only the terminal anatomical changes are available to see there. However, modern methods for intracardiac electrographic studies should help define the temporal rate of progression of rheumatoid heart block.

Finally, both similarities and differences may be noted from comparison of the findings in the cardiac conduction system of these three patients with those in patients dying from disseminated lupus erythematosus,\textsuperscript{27} polyarteritis nodosa\textsuperscript{28} or scleroderma heart disease.\textsuperscript{29} In lupus erythematosus the pericarditis is a more consistently present abnormality and thereby more often affects the sinus node, when one considers all cases; however, in a given patient with either disease plus pericarditis, the effects on the sinus node are the same. Another impressive similarity is the cystic degeneration of the collagen framework of the sinus node.

FIGURE 15. Both the A-V node and His bundle of case 3 were virtually destroyed by focal inflammation and noninflammatory degeneration. The A-V node artery is boxed in A and shown at higher magnification in B. Margins of the A-V node adjacent to the central fibrous body are marked with open arrows in A, and endocardium of the right atrium (RA) is on the left. Note the similarity of the fibromuscular dysplastic narrowing of the A-V node artery here and that shown for case 1 in figure 3.
FIGURE 16. Other areas of focal degeneration and inflammation within the A-V node of case 3 are shown here, along with other segments of the narrowed A-V node artery.

FIGURE 17. These two photomicrographs exhibit the hemorrhage, degeneration and inflammation seen at the junction of A-V node with His bundle in case 3.

seen with lupus erythematosus and particularly in case 2 of the present report. In lupus the arteritis in the sinus node is a conspicuous abnormality and was not a feature in the three present patients; in fact, relative sparing of the sinus node artery was surprising. On the other hand, the focal inflammation and obliterative arterial lesions of the A-V node and His bundle of the three present cases was far more extensive than usually found in lupus erythematosus.

Polyarteritis nodosa seems more regularly to involve both the sinus node artery and the A-V node artery than is the case in rheumatoid arthritis, although the extent of inflammatory involvement of the A-V node artery in case 3 was similar to that seen in patients with polyarteritis. The focal inflammation and degeneration of the A-V node, a finding which was disproportionate to the vascular lesions, seems more a feature of rheumatoid heart disease than of polyarteritis. Involvement of the larger coronary arteries and of many more of the small branches by polyarteritis nodosa was true in my own series and less conspicuous in these three patients with rheumatoid heart disease. However, this may be a sampling error, since others have found more widespread and extensive arteritic lesions in rheumatoid heart disease than I did.

Scleroderma heart disease is conspicuously devoid of inflammation of either the small coronary arteries or of the sinus node and A-V junctional tissues. This is a striking difference from either lupus erythematosus, polyarteritis, or rheumatoid heart disease. Similarly, the excessive amount of collagen deposition and fibrosis of the sinus node in particular (but also the A-V node and His bundle) which is typical of scleroderma heart disease is not seen in either lupus or polyarteritis or rheumatoid heart disease. This noninflammatory collagenosis plus widespread "quiet" (noninflammatory) narrowing of small arteries in scleroderma heart
disease is an intriguing exception in the spectrum of collagen diseases involving the heart. At the same time, one must remember that the three present cases and the others being discussed were chosen because the clinical features in each patient represented rather pure forms of one or the other type of collagen disease. In the usual clinical encounter of patients this type of nosological purity may be the exception rather than the rule. As a corollary, some of these observed histopathological differences should not be overinterpreted when the clinical features of any one patient with collagen disease blur into indistinction.

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