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F. A. DAVIS COMPANY, PHILADELPHIA

Cardiovascular Clinics, 15/3, Sudden Cardiac Death

Printed in the United States of America

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Library of Congress Cataloging in Publication Data

Cardiovascular clinics. 1–

Philadelphia, F. A. Davis, 1969–

v. ill. 27 cm.

Editor: v. 1– A. N. Brest
Key title: Cardiovascular clinics, ISSN 0069-0384
1. Cardiovascular system—Diseases—Collected works. 1. Brest, Albert N., ed.
[DNLM: W1 CA77N]
RC681.A1C27 616.1 70-6558
ISBN 0-8036-5098-1 MARC-S

Library of Congress 75[8307]

Preface

Sudden cardiac death remains one of the most pressing, unresolved problems in Medicine today and remains the major cause of death in patients with coronary artery disease. Over the past 10 years, significant efforts have been made in an attempt to predict those patients at risk for sudden death and to develop pharmacologic and nonpharmacologic methods to prevent patients at risk from dying.

This volume provides a comprehensive review of up-to-date information concerning epidemiology, pathology and underlying mechanisms, and therapeutic interventions possible for the prevention of sudden cardiac death. Holter monitoring and electrophysiologic testing have aided greatly in our understanding of the electrophysiologic milieu that characterizes patients at risk for sudden death. In addition, pharmacologic therapy has been improved with the development of new antiarrhythmic agents as well as the use of both Holter monitoring and programmed stimulation to identify patients at risk and to develop therapeutic regimens. In addition to the pharmacologic therapy of malignant ventricular arrhythmias, the role of implantable electronic devices and surgery in managing these arrhythmias is discussed. Newer methods to predict patients at risk for sudden arrhythmic death are discussed, as well as the potential role of platelets, prostaglandins, coronary spasm, and the autonomic nervous system in the initiation of lethal arrhythmias.

I wish to thank all of the contributing authors for their detailed and well-developed discussion of these topics. I would like to acknowledge the help of the Electrophysiology Fellows and the technical staff at the University of Pennsylvania for helping to generate much of the information published in this book. Special thanks go to Ms. Maria Coscia and Angelika Boyce for assuring the completion of all the authors' manuscripts and meeting all necessary deadlines for this text.

It is my hope that this text will provide the most up-to-date review of all aspects of sudden cardiac death syndrome.

Mark E. Josephson, M.D.
Guest Editor

Editor's Commentary

In years past, cardiac arrest had been invariably fatal. More recently, we have learned how to reverse the condition and how to prevent additional attacks, at least in some instances. Moreover, we have begun to recognize precursors of this disorder. Nonetheless, sudden cardiac death continues to be the leading cause of mortality in the United States. Clearly, therefore, we need to enlarge our understanding of this disorder. This issue of CARDIOVASCULAR CLINICS deals broadly and specifically with the pathology, electrophysiology, pathogenesis, clinical characteristics (initiating events, epidemiology, identification of risks), diagnostic approaches (signal averaging, ambulatory monitoring, programmed electrical stimulation), and management (drug, surgical approaches) of sudden death. The discussions presented in this book by leading authorities in the field suggest that we are on the threshold of firm understanding and of rational dealing with this pervasive problem. I am deeply grateful to Dr. Mark E. Josephson for his guidance in the formulation of this book, and both of us are indebted to the individual authors for their outstanding contributions.

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Contents

The Pathology of Sudden Death*

Saroja Bharati, M.D., and Maurice Lev, M.D.

This chapter deals with the abnormalities in the conduction system and the surrounding structures that may be related to sudden death. We will describe our experience with the pathology found in the sinoatrial (SA) node, the atrioventricular (AV) node, the AV bundle, the bundle branches, the myocardium, the valves, the endocardium, and the anomalous AV connections (in cases of pre-excitation). Our discussion will include case histories of patients in whom we have studied the conduction system.

ABNORMALITIES IN THE SINOATRIAL REGION

Trauma to the SA Node[1]

A 35-year-old woman was believed to have had heart disease since the age of 21. Diagnostic cardiac catheterization studies revealed moderate mitral insuffficiency with marked left ventricular hypertrophy. The pulmonary artery, right ventricular, left ventricular end-diastolic, and pulmonary wedge pressures were elevated. A diagnosis of cardiomyopathy was made. The patient was asymptomatic up to age 35. At that time, she was involved in an automobile accident, and she was unconscious for an unknown period of time. Later, she complained of pain in the right back and the chest. This pain was found to be due to fracture of the right clavicle. Five days later, she collapsed and was found to be in ventricular tachycardia. Subsequent electrocardiograms disclosed paroxysmal atrial tachycardia with varying block and, later, sinus bradycardia with wandering pacemaker from SA node to the AV junction. Twenty-eight days after the accident, she was found dead in bed.

At autopsy, the heart was enlarged, with hypertrophy of both atria and ventricles. At the junction of the left atrium and inferior mitral leaflet close to the posterior commissure, there was a white plaque-like formation measuring 1.5 cm in greatest dimension. This plaque was firm and, on section, showed a tumor-like lesion measuring 0.3 to 0.4 cm in diameter. On section, this plaque was found to consist of benign osteoid tissue. The mitral orifice was enlarged. The coronary arteries revealed moderate atherosclerosis.

Examination of the conduction system revealed a large area of hemorrhage and necrosis in the SA node (Fig. 1), accompanied by macrophages, fibroblasts, and mononuclear cells. Fat tissue partially isolated but did not completely separate the node from the adjacent myocardium. The adjacent epicardium revealed chronic inflammation and hemorrhage. An organiz-

*Aided by Grant HL 30558-02 from the National Institutes of Health, The National Heart, Lung and Blood Institute, Bethesda, Maryland.

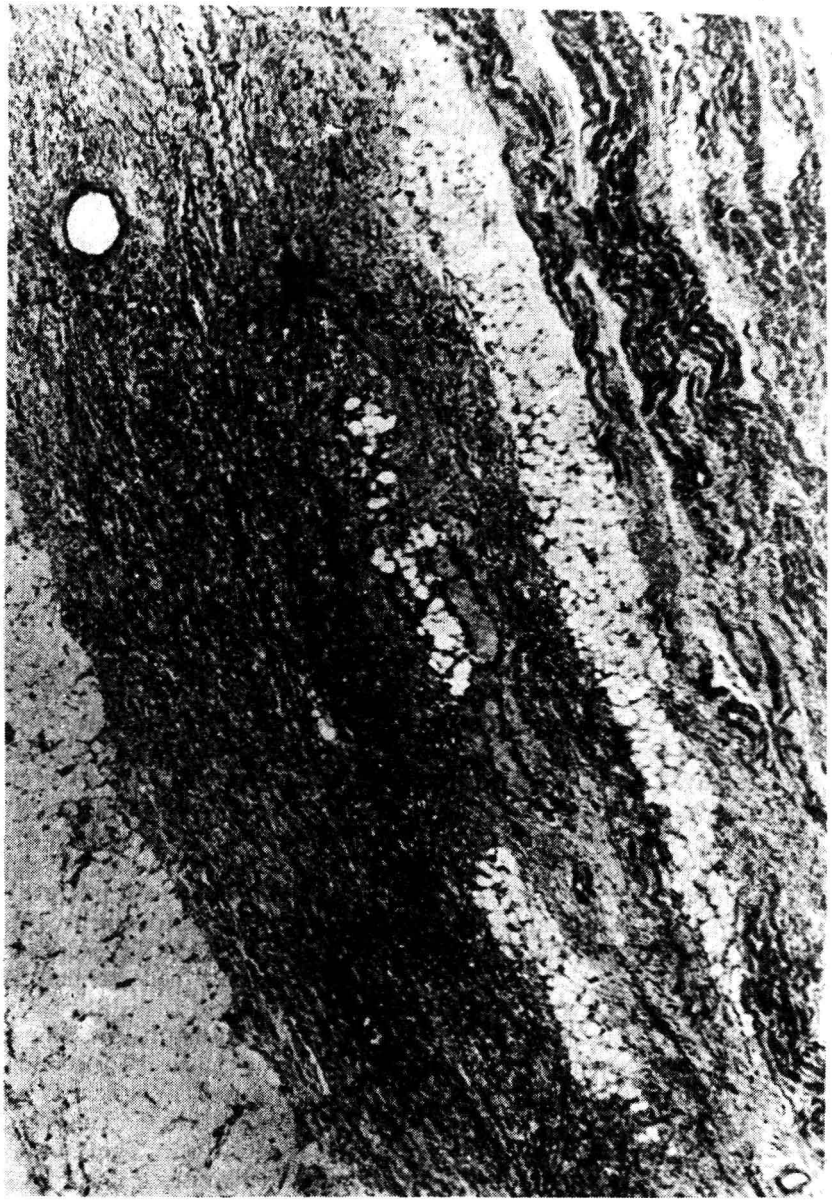

Figure 1. Sinoatrial node showing hemorrhage, with partial isolation of the node by fat tissue. Hematoxylin-eosin stain × 45. (From Bharati et al,[1] with permission.)

ing thrombus was present in the adjacent atrial cavity. The approaches to the SA node showed considerable focal vacuolar and eosinophilic degeneration of muscle cells and moderate fatty infiltration, with a fine infiltration of mononuclear and neutrophilic cells. The atria showed moderate degenerative changes and slight to moderate fibrosis, with chronic organizing pericarditis over the right atrium. The same changes were present in the atrial septum (atrial preferential pathways). The remainder of the conduction system revealed insignificant changes. The ventricles contained spotty areas of old fibrosis.

The bradycardia this patient exhibited for several years before the accident probably was related anatomically to the partial separation of the SA node by fatty tissue. The atrial preferential pathways and the approaches to the SA node also revealed some chronic changes. The atrial arrhythmias associated with the collapse of the patient subsequent to the automobile accident were probably related to the hemorrhage in the SA node. This hemorrhage was most likely traumatic in nature. Thus, nonsurgical blunt trauma to the chest wall may result in hemorrhage in the SA node, which may cause various types of atrial arrhythmias and may terminate in sudden death. Likewise, one may hypothesize that if extensive hemorrhage were to occur (as a result of any type of nontraumatic injury to the chest wall) in the region of the AV node, AV bundle, or bundle branches, various types of tachyarrhythmias or bradyarrhythmias or both might result and lead also to sudden death.

Sick Sinus Syndrome in Younger Age Groups[2]

Although the sick sinus syndrome in young individuals is uncommon and generally well tolerated, it may precipitate a bradyarrhythmic or tachyarrhythmic syndrome that could result in sudden death.

A 16-year-old boy had a harsh systolic murmur at birth. At 11 months, cardiac catheterization revealed a left-to-right shunt at the ventricular level. At 6 years of age, the murmur was not audible, and at 13 years of age, repeat cardiac catheterization was found to be normal. At the age of 5 years, the boy had syncopal attacks and convulsions. Apparently he was asymptomatic thereafter. However, at the age of 14 years, he was evaluated for bradyarrhythmias. He died suddenly at age 16. At 2 years of age, electrocardiograms disclosed sinus tachycardia interrupted by sinus pauses of 1.3 to 1.4 sec. Subsequent electrocardiograms at the ages of 7½ and 8½ years showed normal sinus rhythm. At age 13 years, electrocardiograms showed brief runs of supraventricular tachycardia followed by pauses of 1.5 to 1.7 sec, terminated by junctional escape rhythm, with rates of 40 to 50 beats per min. An electrophysiologic study at the age of 14 years revealed a junctional escape rhythm (cycle length of 1040 msec) that controlled both the atria and ventricles (H–V interval 40 msec). The SA recovery time, determined by atrial pacing, was prolonged. After administration of atropine, the SA recovery time increased. After the study, the patient failed to keep his medical appointments but was reported to have pulse rates of 70 to 90 beats per min during school examinations.

At postmortem examination, there was gross evidence of spontaneously closing ventricular septal defect. The SA nodal artery showed no changes, and there were only minimal changes in the SA node itself. However, the approaches to the SA node showed marked fibrosis (Fig. 2), and diffuse fibrosis was found in the anterior, middle, and inferior preferential pathways. Likewise, the approaches to the atrioventricular node revealed considerable fibrosis. The sinusoids and lymphatics were dilated. The AV node showed moderate fibrosis. The AV bundle was markedly septated. The left bundle branch was disrupted at the region of the bifurcation. This latter region, which revealed considerable fibroelastosis, was the location of the closing ventricular septal defect. The summit of the ventricular septum revealed marked fibrosis, especially in the region of the ventricular septal defect. Likewise, the right bundle branch revealed fibrosis at the region of the closing ventricular septal defect.

In summary, the approaches to the SA node and AV node, and the atrial preferential pathways, were altered by fibrosis in this case. This fibrosis apparently resulted in sick sinus syndrome. The cause of this fibrosis is unknown.

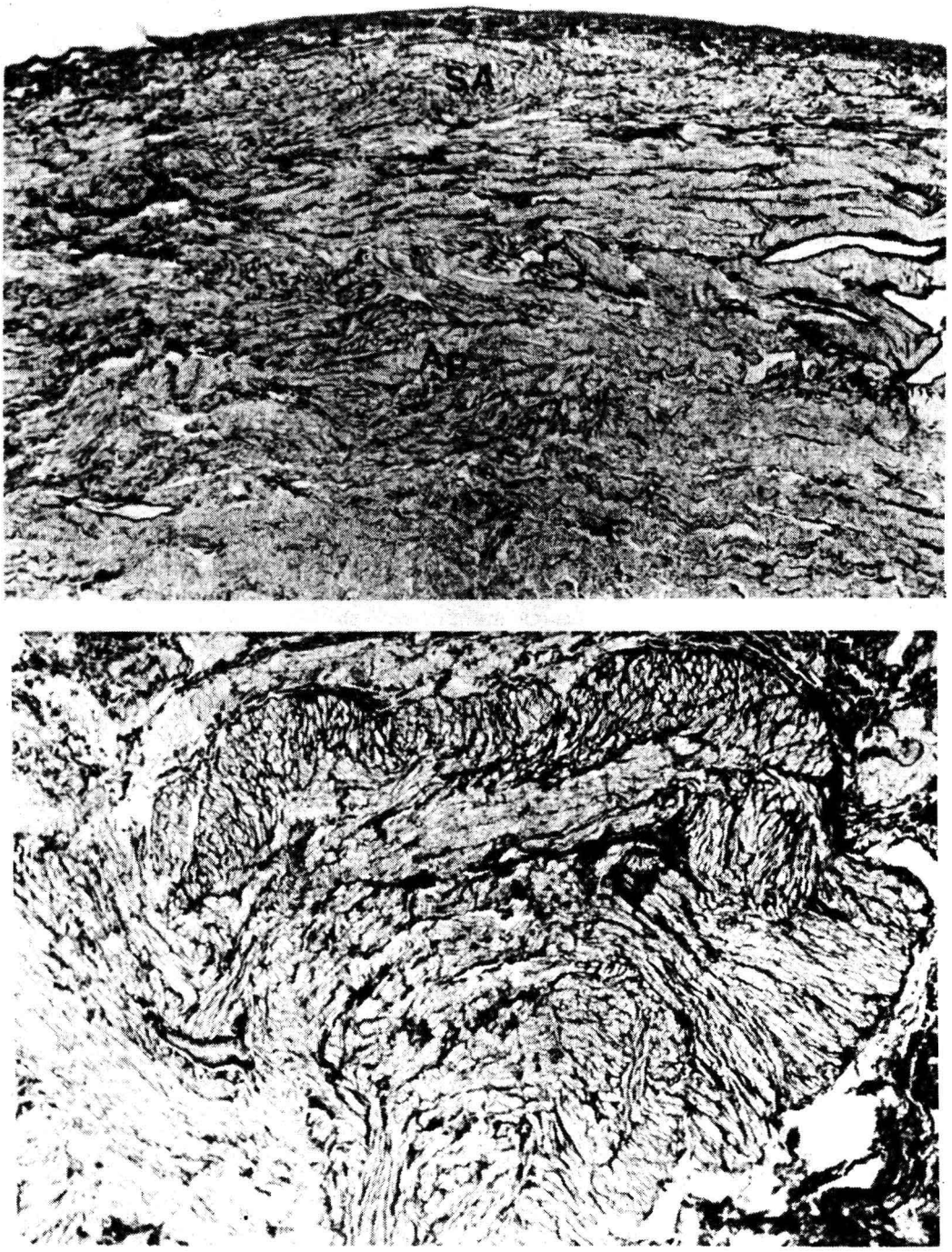

Figure 2. *(Top)* Sinoatrial node and approaches; *(bottom)* superior approaches to SA node showing marked fibrosis. Ap = approaches to sinoatrial node; SA = Sinoatrial node. Weigert-van Gieson stain × 45 (both top and bottom). (From Bharati et al,[2] with permission.)

Sick Sinus Syndrome in the Aged[3]

This disorder may manifest itself clinically as the tachycardia-bradycardia syndrome. The latter consists of paroxysmal atrial fibrillation, flutter, or tachycardia followed by SA block or sinus arrest, resulting in Stokes-Adams attacks.

A 74-year-old white man with senile dementia was hospitalized for dizziness and syncope. At admission, the electrocardiogram revealed paroxysmal atrial fibrillation, followed by atrial arrest and depression of the AV junctional pacemaker. In addition to the cardiac rhythm abnormalities, the electrocardiogram revealed evidence of recent ischemia of the anterior, lateral, and posterior walls superimposed on a pattern of left ventricular hypertrophy. Because of the patient's severe senile dementia, a pacemaker was not implanted. The patient died suddenly the following day.

At autopsy, there was a recent thrombus in the left circumflex coronary artery, a huge recent infarct of the proximal two thirds of the posterior ventricular septum, and rupture of the posterior and lateral walls. Some arterioles in the SA node showed marked narrowing, acute degeneration, or necrosis. There was also mononuclear cell infiltration, with focal areas of fibrinoid necrosis of collagen. The approaches to the SA node showed considerable fibrosis and elastosis. Chronic pericarditis was present, involving the adjacent myocardium and the nerve trunks. Examination of the SA nodal artery revealed acute degeneration but no narrowing. There were acute and chronic inflammation, arteriolosclerosis, and necrosis in the approaches to the AV node. Acute degeneration of the AV nodal artery was found. The AV node showed chronic inflammation and proliferation of sheet cells. The AV bundle showed acute degeneration as well. Thus, the sudden death in this patient, although produced by the recent infarct, may have been related to the sick sinus syndrome. This syndrome in the aged is often accompanied by ischemic heart disease.

ABNORMALITIES IN THE AV NODAL REGION

Sudden Death Caused by a Benign Tumor (Mesothelioma) of the AV Node[4]

Although mesothelioma of the AV node is benign, it may cause sudden cardiac death related to its location. We have encountered two such cases in our material. We will discuss one particular case in some detail.

A 16-year-old girl, gravida 1, para 1, was hospitalized for cardiac catheterization and evaluation for pacemaker insertion. Six weeks before admission, she gave birth to a normal infant. Immediately postpartum, her heart rate fell to 35 beats per min and her electrocardiogram disclosed 2:1 AV block, with intermittent complete heart block. She was transferred to the coronary care unit and eventually discharged on isoproterenol, with the intention of having her return in 6 weeks for further evaluation of her cardiac condition. Her history revealed that she had two episodes of syncope during her pregnancy. These episodes were apparently similar to the three or four syncopal episodes she had experienced at 9 and 11 years of age in school.

At the time of hospitalization, she had a regular heart rate of 45 beats per min, and the electrocardiogram revealed complete heart block with atrial rates between 70 and 100 beats per min. The ventricular escape rate averaged 45 beats per min. The escape rhythm was junctional with a narrow QRS complex of normal morphologic features. His bundle electrograms revealed complete block proximal to the His bundle. The escape beats were all preceded by His bundle potentials with a normal H–V interval of 40 msec. Diagnostic cardiac catheterization disclosed normal pressures. The patient had an asystolic cardiac arrest during cardiac catheterization, and she could not be resuscitated.

The conduction system of the heart revealed that the distal portion of the atrial septum was replaced by a tumor mass. The AV node was almost completely replaced by the tumor