Specialty Conference

Participants

MELVIN M. SCHEINMAN, MD*
ROBERT PETERS, MD
DAVID S. HIRSCHFELD, MD
JOSEPH A. ABBOTT, MD†
FRED KUNKEL, MD

Refer to: Scheinman MM, Peters R, Hirschfeld DS, et al: The sick sinus and ailing atrium—Teaching Conference, San Francisco General Hospital and University of California, San Francisco (Specialty Conference). West J Med 121:473-481, Dec 1974

The Sick Sinus and Ailing Atrium

ROBERT PETERS, MD:‡ The human sinus node is a small ovoid structure located at the junction of the superior vena cava and right atrium. The artery to the sinus node courses through the center of the node and the node has aptly been described as an "enormous adventitia" of the artery.[1] The node itself is composed of a dense collagenous framework that is attached to the central artery and clusters of interlacing fibers.[2] The fibers contain predominately two types of cells—cells with large ovoid nuclei and few myofibrils (P cells) and cells intermediate in histologic structure between P cells and atrial myocardial cells. The sinus node tracts merge, especially at the periphery of the node, and form large Purkinje-like tracts that course through the atrial myocardium. The P cells are thought to be the site of impulse generation, while the perinodal fibers probably serve to amplify and synchronize the impulses arising from the sinus node cells.[3]

Normally, the sinus node is the dominant cardiac pacemaker because its discharge rate is more rapid than the other automatically discharging cells within the heart. Because the sinus node discharge rate must ordinarily vary greatly to meet body needs, it is not surprising to find that it is richly innervated by postganglionic sympathetic and parasympathetic fibers.

Disease of the sinus node may become manifest by abnormalities in impulse generation and/or impairment of impulse conduction through the sinoatrial junction. Relatively few detailed histologic studies are available for patients with sinus node dysfunction. These studies[4-7] and other electrophysiologic studies[8,9] would suggest that these patients commonly have disease not only of the sinus node but also of the approaches to the sinus node, the atrium, the atrioventricular (A-V) node, and the ventricular specialized conduction system.

We have divided this discussion into four sections. Dr. Hirschfeld will explore the clinical and electrocardiographic features, Dr. Abbott will discuss the importance of exercise stress testing, Dr. Kunkel will describe the electrophysiologic testing and Dr. Scheinman will conclude by discussing the management of patients with sinus node disease.

Clinical and Electrocardiographic Features

DAVID S. HIRSCHFELD, MD:§ Twenty-eight patients with symptoms and electrocardiographic evidence of sinus node dysfunction were observed for a

From the Medical Service, San Francisco General Hospital, and the Department of Medicine and the Cardiovascular Research Institute, University of California, San Francisco.

Supported in part by Grant HL 06285, National Institutes of Health, Bethesda, Maryland.

*This study was performed during tenure of the American Heart Association Teaching Scholar in Cardiology.

†Supported in part by Alfred Stengel Traveling Scholarship of the American College of Physicians.

‡Clinical Instructor in Medicine, University of California, San Francisco; member of staff, San Francisco General Hospital.

Reprint requests to: M. M. Scheinman, MD, Medical Service, San Francisco General Hospital, 1001 Potrero, San Francisco, CA 94110.

§Cardiology Fellow, University of California, San Francisco, School of Medicine; Medical Service, San Francisco General Hospital.

TABLE 1.—*Clinical Spectrum of Patients with Sinus Node Disease*

Symptoms and Cardiovascular Diagnosis	*Number of Patients*			
	Sinus Bradycardia	*Bradycardia-Tachycardia Syndrome*	*Sinus Arrest*	*Total*
Number in group	13	11	4	28
Syncope	8	4	4	16
Near syncope	1	3	0	4
Angina	3	1	0	4
Palpitations	0	4	0	4
Conduction defect*	4	4	1	9
Congestive heart failure	5	5	1	11
Hypertension	6	1	0	7
Previous history of myocardial infarction	3	3	0	6
Cerebrovascular accident	3	0	0	3
Cardiac amyloidosis	0	2	0	2

*Either PR prolongation or bundle branch block or hemiblock pattern.

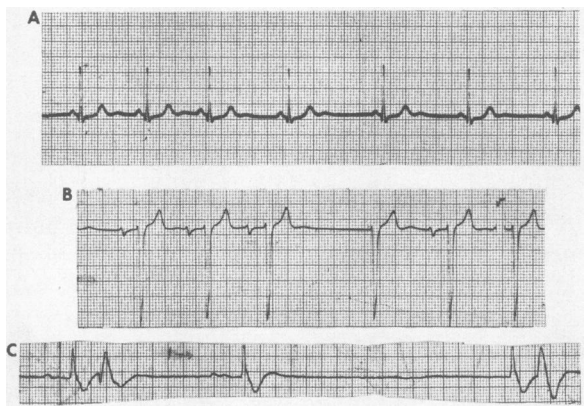

Figure 1.—Representative electrocardiograms from patients with symptomatic sinus bradycardia (Group I). **A,** after the third complex, there is abrupt slowing of the sinus rate. **B,** sinus exit block. Three sinus beats are followed by a pause that equals 3 P-P intervals. The fourth QRS complex is an escape junctional beat. **C,** the first and third complexes are sinus beats, after which a sinus pause of 3½ seconds is terminated by a junctional escape beat.

mean period of 18 months. All of them underwent prolonged continuous electrocardiographic monitoring either in a coronary care unit or by means of a continuous tape memory loop (Holter) system. Only patients with chronic rhythm disturbances were included, and patients with sinus bradycardia that may have been related to drugs, electrolyte imbalance, thyroid dysfunction or acute myocardial infarction were excluded from this study.

The mean age for the group as a whole was 54±19 years and the range was from 10 to 80 years. The age distribution appeared to be bimodal with one peak at a mean age of 31 and a second peak at 63 years. Sixteen men, one boy, and eleven women were studied. The group was further subdivided into three subgroups on the basis of the major cardiac rhythm disturbance found (Table 1). Group I consisted of 13 patients with sinus bradycardia that was defined as a persistent resting heart rate below 55 beats per minute. Electrocardiographic rhythm strips in 11 patients (Group II) showed alternating sinus bradycardia and tachycardia. Finally, electrocardiograms of four patients (Group III) showed periods of sinus arrest, defined as cessation of all atrial activity associated with cardiac asystole for at least 5 seconds. Although each patient was assigned to a group on the basis of the predominant rhythm disturbance found, considerable overlap in the type of arrhythmias was observed among patients in the three groups. The pertinent clinical data are summarized in Table 1.

Near syncope or syncope was the most common symptom (9 of 13 patients) for patients with symptomatic sinus bradycardia (Group I). The most common rhythm disturbance for patients in this group (and in Groups II and III) consisted of episodic sinus slowing—with or without evidence of sinus node exit block—(Figure 1A and B). The sinus slowing was often followed by escape junctional or ventricular beats (Figure 1C). Only one patient in this group required a permanent intracardiac pacemaker for control of heart failure. In the remaining patients in this group symptoms of left-sided cardiac failure were well controlled with digitalis and diuretic therapy.

Supraventricular arrhythmia including paroxysmal atrial or junctional tachycardia and atrial fibrillation or flutter was observed in ten patients with bradycardia-tachycardia syndrome (Group II). One patient with multiple myeloma and persistent sinus bradycardia (alternating with a slow

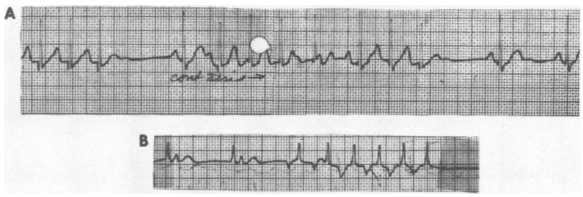

Figure 2.—Representative electrocardiograms from patients with supraventricular arrhythmias (Group II). **A,** an episode of paroxysmal atrial tachycardia terminates spontaneously. After a sinus beat (fourth complex), atrial tachycardia with Mobitz I atrioventricular block resumes. **B,** a junctional rhythm is interrupted by an episode of paroxysmal atrial tachycardia (third complex).

junctional rhythm) had recurrent bouts of ventricular tachycardia requiring electroconversion. The onset of the tachycardia was recorded in six patients, and in all recorded instances the tachyarrhythmia was initiated by a premature supraventricular beat and never observed to begin after a prolonged sinus pause. Two examples of this phenomenon are illustrated in Figure 2. Bouts of supraventricular arrhythmia were often followed by a prolonged pause terminated by atrial or junctional escape beats. On follow-up, stable atrial fibrillation developed in one patient and it was well controlled with digitalis therapy. Three patients required insertion of a permanent right ventricular pacemaker for control of severe symptomatic sinus bradycardia, recurrent ventricular tachycardia, or Stokes-Adams attacks resulting from 3° A-V block. The patient with multiple myeloma died because of repeated pulmonary embolization.

One patient in the group with sinus arrest (Group III) had recurrent syncopal episodes and cardiac arrest owing to sinus arrest, and cardiac asystole was documented on two occasions (Figure 1C). This patient, however, had a regular sinus rhythm and normal heart rate during prolonged repeated monitoring in a coronary care unit and during a 12-hour Holter recording. One patient had persistent sinus bradycardia, and the remaining two patients had alternating sinus bradycardia, supraventricular tachycardia, and cardiac arrest owing to sinus arrest and cardiac asystole. The four patients in this group all required permanent intracardiac pacemakers. Of particular interest was one patient in this group who continues to have symptoms of presyncope even after insertion of a normally functioning demand right ventricular pacemaker.

Several clinical features of this disease entity deserve emphasis. Contrary to prevailing belief, sinus node dysfunction is not limited to the elderly;[5,10] our youngest patient, for example, was ten years of age, and one-third of our subjects were less than 50. Although coronary artery and hypertensive cardiovascular diseases are commonly associated conditions[10-12] (Table 1), the paucity of detailed histologic studies makes a causal link rather tenuous. Clinical,[5,8,10,11,13] electrophysiologic,[14] and histologic[4] studies have conclusively demonstrated associated disease of both the A-V node and the ventricular specialized conducting system in many patients with sinus node disease. This finding has important therapeutic implications with regard to the site of pacemaker implantation. Finally, although the natural history of this disease is still unclear,[15] there appears to be wide variability in severity of symptoms and progression of disease. Fortunately, deaths due to arrhythmia appear to be uncommon.[5,10,13]

In summary, most patients with sinus node disease may be diagnosed by scrutiny of electrocardiographic rhythm strips. In our experience, the most common finding is persistent sinus bradycardia, oftentimes associated with periods of gradual further slowing of the sinus rate and escape of a lower pacemaker. Some patients also show cardiac arrest resulting from sinus arrest and cardiac asystole, while others show an alternating bradycardia-tachycardia arrhythmia.

Exercise Stress Testing

JOSEPH A. ABBOTT, MD:* Syncope, tachyarrhythmia, and cardiac arrest are well known manifestations of the sick sinus syndrome.[16] Because of the advanced age of many patients with the sick sinus syndrome and the tendency of the elderly to lead less physically active lives the effort-induced disabilities these subjects suffer are less well appreciated.[17,18] We performed both autonomic screening and exercise tests in nine control subjects and 15 of the patients previously described by Dr. Hirschfeld. Most were young and physically active and were without clinical evidence of myocardial disease. Both the exercise and autonomic studies were thoroughly explained and an informed consent statement was signed by each patient and control.

Nine male and six female patients with the sick sinus syndrome, ranging in age from 10 to 77 years (mean 47 years), and nine control subjects were

*Associate Clinical Professor of Medicine, University of California, San Francisco, School of Medicine; Assistant Director, Cardiopulmonary Unit, San Francisco General Hospital.

exercised on a bicycle ergometer,* using a technique that allows serial measurement of heart rate and oxygen consumption at incremental levels of exercise.[19] The study groups included patients in each of the three previously described categories: five patients in Group I, six patients in Group II, and four patients in Group III. Five patients had functioning permanent demand ventricular pacemakers at the time of the study. Patients who were poorly motivated, had orthopedic limitations, severe lung disease, unstable angina, or a recent myocardial infarction were excluded from exercise evaluation. Control subjects were matched as to sex and age with the study group and included staff physicians, medical interns and residents, and laboratory technicians. Exercise was stopped when patients expressed a desire by signaling the physician or when they developed objective evidence of untoward cerebral or cardiac symptoms—lightheadedness, breathlessness, arrhythmia, or fainting. No untoward effects were noted in control subjects and effort was terminated when 90 percent of the age-predicted maximum heart rate was achieved.

Since dysfunction of the autonomic system may be present in patients with the sick sinus syndrome, autonomic screening tests including the Valsalva maneuver, carotid sinus massage, and measurement of blood pressure and heart rate in supine and upright positions were performed before the exercise tests.[15,20-23] After a 15-minute recovery period from exercise, 1.0 mg of atropine sulfate was administered intravenously over a 5-minute period during which the heart rate was recorded.[24]

The resting heart rates of the patients in Group I (46±6 beats per minute) and Group II (50±10 beats per minute) were significantly below the resting heart rates of control subjects (78±10 beats per minute) or patients in Group III (72±11 beats per minute) in whom ventricular demand pacemakers were set at rates of approximately 70 beats per minute. With exercise, patients with sinus node disease were unable to achieve heart rates comparable to those in control subjects (Chart 1). The differences were statistically significant ($p<0.05$), even though the normal subjects were only stressed to 90 percent of their maximum predicted heart rate. Mean resting oxygen consumption was similar in control

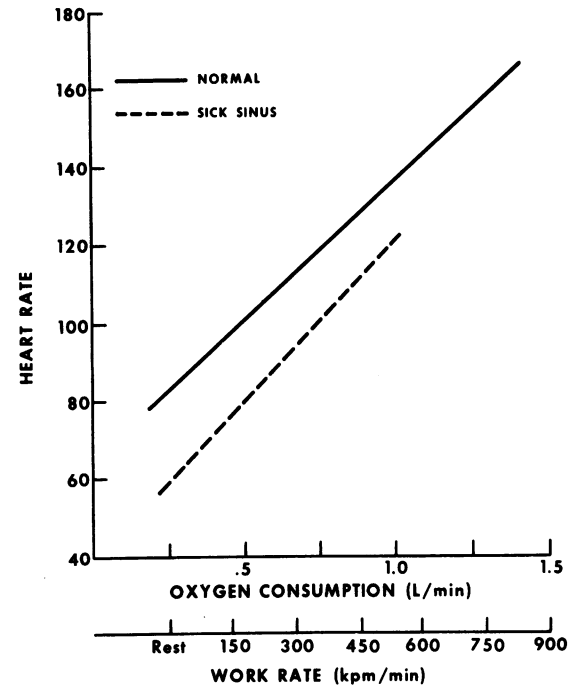

Chart 1.—Resting and maximal exercise oxygen uptake and work rates are plotted against heart rate. The curve of the 15 patients with sinus node disease lies to the right of the curve for control subjects. Both heart rate response and the work performance level (maximal oxygen uptake) are blunted in patients with sinus node disease.

(0.195±0.05 liters per minute) and patients (0.210±0.08 liters per minute) groups. Mean oxygen consumption at maximum stress (Chart 1) was significantly lower for patients (1.01±0.18 liters per minute) compared with predicted maximum oxygen consumption for control subjects (1.65±0.31 liters per minute) ($p<0.005$). Similarly, work levels achieved at the termination of exercise were significantly lower for patients (mean 450 kg-meters per minute) than for control subjects (mean 900 kg-meters per minute) ($p<0.05$). Six of the patients had permanent or temporary demand ventricular pacemakers inserted to prevent syncope or to treat symptoms of heart failure. In each the pacemaker rate had been set between 65 and 70 beats per minute. When exercise performance of these patients was compared with that of the subgroup of patients without pacemakers, there was no significant difference in maximum exercise oxygen uptake and none of the patients with ventricular pacemakers had relief from their exercise-induced symptoms. The reason for termination of exercise was dizziness, which was often related to cardiac arrhythmia, to development or worsening of symptoms of con-

*Bicycle ergometer Model AM368, Elema Schonander, Stockholm, Sweden.

TABLE 2.—*Exercise-Induced Signs and Symptoms in Patients with Sinus Node Disease*

	Number of Patients with Signs and Symptoms					
Group Number	*Development or Worsening of Heart Failure*	*Fatigue*	*Angina*	*Faint*	*Dizzy*	*Arrhythmias Noted*
I	2	1	1	1	0	0
II	0	1	0	0	4	Atrial flutter Ventricular tachyarrhythmia Atrial fibrillation
III	1	2	0	0	2	0

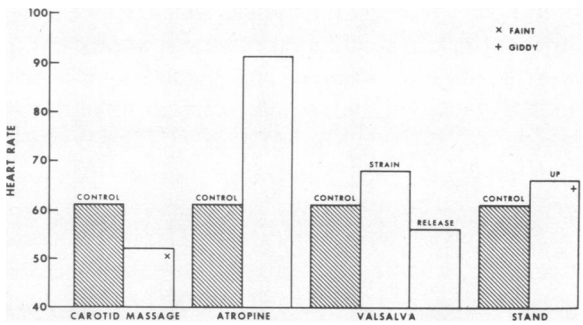

Chart 2.—The heart rate responses to autonomic screening are charted in 15 patients with the sick sinus syndrome. The heart rate responses are qualitatively normal for each test maneuver. However, the changes in heart rate were less than those observed for the normal subjects. In three instances abnormal responses were associated with cerebral symptoms (faintness with carotid massage in two instances and giddiness with hypotension on tilting in one).

gestive heart failure, exhaustion, or angina; exercise-induced arrhythmias were noted only in the patients in Group II. These findings are detailed in Table 2.

Patients with sick sinus disease clearly show abnormal exercise stress performance.[25,26] This finding may be owing to several factors:[27] the patients may have been in poor physical condition, had impaired myocardial function or autonomic dysfunction or both, or had end organ (sinus node) disease. Any or all of these alternatives could prevent the normal acceleration of the sinus node rate to meet body needs. Subjects in poor physical condition show an increased heart rate for any given level of exercise; our patients had heart rates lower than control subjects for each exercise load. Exercise performance in the control group, in fact, fell into an "unfit" category.[28] Thus, the differences in work performance between the patients and the control subjects were not owing to differences in physical conditioning. Although 10 of 15 patients (67 percent) had no clinical evidence of cardiac disease, the inability of the patients to achieve maximum oxygen consumption and work rate levels may well have resulted from an inability to increase stroke volume to compensate for a blunted increment in exercise heart rate.[29]

Autonomic screening is an important part of the evaluation of the patient with sick sinus disease. In our study the screening procedures used involved those tests that could readily be performed at the bedside, including carotid massage, Valsalva's maneuver, tilting, and electrocardiographic monitoring before and after intravenous injection of atropine sulfate.[30] The effects of these procedures are summarized in Chart 2. In brief, these patients showed a somewhat blunted but qualitatively normal response in heart rate and blood pressure. In two patients carotid sinus massage led to an inordinate slowing of the heart rate and a fall in blood pressure and was associated with near syncopal symptoms. Another patient, a 60-year-old diabetic woman who required a permanent demand ventricular pacemaker to prevent recurrent cardiac asystole owing to sinus arrest, first presented with fainting spells, and pacemaker malfunction was suspected. Subsequent complete autonomic testing revealed a mixed parasympathetic and sympathetic disorder. Her symptoms of recurrent cardiac arrest resulted from sick sinus disease, which had been adequately managed by a demand ventricular pacemaker. Her autonomic disorder was responsible for her postpacemaker "drop attacks" and mimicked pacemaker malfunction.

In summary, physiologic stress testing and autonomic screening procedures may be of great clinical value in the evaluation of patients with symptomatic sinus node disease. Primarily, serious arrhythmias may be uncovered by exercise stress testing, which may lead the clinician to institute specific antiarrhythmic therapy or suggest limitation of strenuous activities. In addition, while pacemaker therapy is eminently successful in the

prevention of bradyarrhythmias and syncope, our studies clearly show that such therapy is ineffective in abolishing exercise-induced symptoms; thus, patients who are young and active should properly be forewarned before insertion of a pacemaker. Finally, since autonomic disease may mimic or exacerbate symptoms in patients thought to have sinus node disease, careful evaluation of the autonomic nervous system is essential; autonomic dysfunction may require additional therapeutic management.

Electrophysiologic Testing

FRED KUNKEL, MD:* Various electrophysiologic abnormalities have been found in patients with sinus node disease. Abnormal prolongation of post-pacing depression of sinus node automaticity (sinus node recovery time) commonly occurs in patients with sinus node dysfunction.[15] This test is thought to test the generator function of the sinus node.[31] Strauss et al[32] suggested use of coupled electrically induced atrial depolarizations to measure sinoatrial conduction time. Coupled atrial beats (A_1A_2†) induced late in the atrial cycle (that is, greater than 75 percent of the spontaneous cycle length, A_1A_1†) result in progressive linear prolongation of the subsequent return cycle (A_2A_3†). This has been designated as Zone I by Strauss and his colleagues.[32] During Zone I, the sinus node is not depolarized or "reset," and the test cycle (A_1A_2) plus the subsequent return cycle (A_2A_3) is equal to twice the spontaneous cycle length (A_1A_1). Progressively earlier coupled atrial depolarizations, however, result in return cycles of similar length (Zone II), which is ascribed to premature depolarization or "resetting" of the sinus node. In Zone II, since the sinus node is reset, A_1A_2 plus A_2A_3 is less than twice A_1A_1. The difference between A_2A_3 and A_1A_1 during Zone II and hence the point in the A_1A_1 cycle at which Zone I changes to Zone II has been suggested as another index of sinoatrial conduction time. Therefore, if the conduction time into the sinus node were prolonged, Zone I would constitute a greater proportion of the return cycle and A_2A_3 during Zone II would be abnormally lengthened. Strauss and coworkers[32] found one patient with sinus node disease who never reached Zone II, and they defined this phenomenon as 1° sinus node entrance block. In our studies we measured the effective atrial refractory period in addition to the tests just described. The effective refractory period of the atrium is defined as the shortest interval between the spontaneous (or driven atrial beat) atrial depolarization and the coupled electrical impulse that results in atrial depolarization.[33]

Twenty-one of our 28 patients underwent these electrophysiologic tests in order to better define sinus node and atrial function as well as to measure atrioventricular conduction times. In addition, 15 control subjects without any evidence of sinus node dysfunction (who were referred to our laboratory for atrial pacing as part of their evaluation for chest pain) were also studied. Informal written consent, according to a protocol approved by the University Committee on Human Experimentation, was obtained from each patient before the study. A quadripolar electrode catheter was inserted against the high lateral right atrial wall for purposes of atrial pacing. An additional electrode catheter was inserted into a femoral vein and positioned across the tricuspid valve for recording the His bundle deflection.[34] Sinus node recovery times were obtained after abruptly terminating atrial pacing at rates of 100 and 120 beats per minute. The atrial cycle was then scanned (as described) by means of single electrically induced coupled atrial depolarizations at various intervals after spontaneous atrial depolarizations. Finally, the effective atrial period was determined at varying paced atrial rates.

The sinus node recovery time (interval from last paced atrial beat to the next spontaneous atrial depolarization) was prolonged in 16 of the 21 patients (Chart 3). The longest sinus node recovery time in the control group was 1,230 msec. The results of atrial scanning are summarized in Chart 4. Simultaneous plots of test (A_1A_2) versus return (A_2A_3) cycles showed three types of curves. The "normal" curve shown in the cross-hatched area shows both Zones I and II as described previously. Zone II was reached at a mean A_1A_2 interval of approximately 80 percent of the control cycle length. Two patients with sinus node disease showed abnormal curves (one of these patients had a normal sinus node recovery time): in one, Zone II was never achieved (1° sinus node entrance block), and in the other, Zone II was achieved at A_1A_2 intervals of less than 50 percent of the spontaneous cycle length. Five of the 21

*Research Fellow, Cardiovascular Research Institute, University of California, San Francisco.

†A_1A_1 = spontaneous cycle length, A_1A_2 = interval from spontaneous atrial beat to coupled atrial depolarization, and A_2A_3 = interval from induced atrial premature beat to the next spontaneous atrial beat.

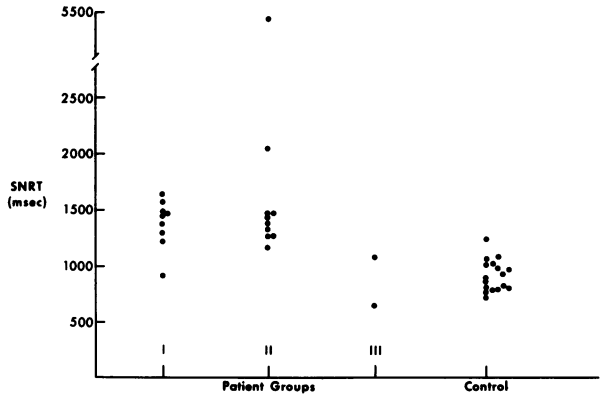

Chart 3.—Sinus node recovery times (SNRT) for the three groups of patients with sinus node disease and for control subjects following atrial pacing at 100 beats per minute. Sixteen of 21 patients with sinus node disease showed abnormally prolonged SNRT.

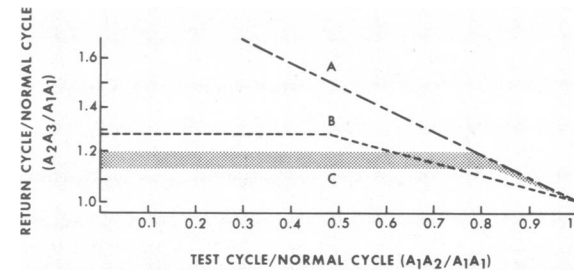

Chart 4.—Relationship between test (A_1A_2) and return cycles (A_2A_3). The numbers 1.0 on the ordinate and abscissa, through which lines are drawn, represent the corrected spontaneous atrial cycle length of each person tested ($A_1A_1/A_1A_1=1.0$). Points along the abscissa represent fractions (in tenths) of A_1A_1 at which premature atrial beats were placed (test cycle on A_1A_2). For each A_1A_2 interval, the recovery cycle (A_2A_3) was also recorded and expressed as a fraction (in tenths) of A_1A_1. Thus, recording the corrected recovery time (A_2A_3/A_1A_1) for every corrected test cycle (A_1A_2/A_1A_1) allows for direct comparison of patients with different cycle lengths. Cumulative points of test (A_1A_2) and return cycles (A_2A_3) for all subjects are shown. A and B are the two abnormal curves and C is the composite "normal" curve points.

patients showed abnormal prolongation of the atrial effective refractory period (even when corrected for cycle length);[35] however, all five showed prolonged sinus node recovery time. One patient with a persistent slow junctional rhythm showed no spontaneous atrial depolarization or contraction (by fluoroscopy), and the atrium was inexcitable despite repeated attempts to pace from different positions in the right atrium with maximum current flow of 25 milliamperes.

The study design allowed for evaluation of both sinus node and atrial function as well as A-V nodal and infranodal conduction. Abnormalities in A-V nodal conduction as determined by prolongation of the interval from the low right atrial electrogram to the His deflection[36] or by A-V nodal block induced by atrial pacing was found in six patients with sinus node disease. Prolongation of infranodal conduction (interval from His deflection to the onset of ventricular activation)[36] was found in five.

In summary, electrophysiologic testing is important in both substantiating the diagnosis of patients with sinus node dysfunction and in determining the site for pacemaker implantation. Seventeen of the 21 patients showed some abnormality in generator function, sinoatrial conduction, or atrial refractoriness. Clearly, the most sensitive and specific test was the sinus node recovery time, which was abnormally prolonged in 16 of the 21 patients with sinus node disease. Normal sinus node recovery time may occur in patients with sinus node disease, presumably because of the block of entry of driven atrial beats into the sinus node.[32] Two patients showed abnormalities in sinoatrial conduction, and one of these patients had normal sinus node recovery time; one patient showed atrial inexcitability. Likewise, a significant number of patients with sinus node disease (45 percent) showed abnormalities in A-V conduction. If permanent pacemaker insertion is necessary, then obviously a ventricular rather than an atrial pacemaker is indicated for patients showing significant abnormalities in A-V conduction.

Management of Patients

MELVIN M. SCHEINMAN, MD:* The wide variability in both symptoms and courses of patients with sinus node disease necessitates careful individualization of both the evaluative testing just described and the therapy. In patients with sinus bradycardia or sinus arrest or both, associated with recurrent bouts of syncope, intracardiac pacemaker therapy is clearly indicated.[12] Rationale for the different types of pacemakers employed will be discussed later. Quite clearly, drug therapy (isoproterenol or belladonna derivatives) is ineffective for long term control of these cardiac arrhythmias;[16] however, digitalis may be used to control symptoms of congestive heart failure in patients with sinus bradycardia.[10] On the other hand, many patients will present with electrocardiographic findings of sinus bradycardia and a history of episodic symptoms (for example, giddiness, syncope, angina). For these patients prolonged electrocardio-

*Associate Professor of Medicine, University of California, San Francisco, School of Medicine; Chief, Coronary Care Unit, San Francisco General Hospital.

graphic taped (Holter) monitoring may prove invaluable in detecting episodic severe sinus slowing or arrest associated with the symptoms or both. If prolonged electrocardiographic monitoring fails to reveal sinus slowing or arrest, then the evaluative tests described herein may be quite helpful in detecting sinus node dysfunction. Our experience suggests that an integrative approach utilizing tests to evaluate the autonomic nervous system, exercise stress testing, and studies of the sinus node recovery time, sinus node conduction time, and atrial refractoriness may help distinguish patients with sinus node dysfunction from patients with sinus bradycardia resulting from hypervagotonia. In general, patients with sinus node disease show a blunted response as to changes in heart rate after atropine administration as well as the Valsalva or upright tilt procedures and exercise. Persons with hypervagotonia, however, show a brisk increase in heart rate after administration of atropine and a normal increase in heart rate and cardiac output during exercise stress testing.[20] Finally, the vast majority of our patients showed abnormalities in electrophysiologic stress testing designed to evaluate sinus node generator function, sinoatrial conduction time, or atrial refractoriness, or both. The finding of one or more abnormalities on testing does not necessarily dictate the need for insertion of a permanent intracardiac pacemaker; rather, this decision is made on the basis of the seriousness of the patient's symptoms. It is well appreciated that the symptom-free interval may last for many years,[10,16] and, furthermore, symptoms may be relatively minor (episodic fatigue, giddiness) and well tolerated. In our view, only patients with documented sinus node disease and at least one clear-cut syncopal episode should undergo insertion of a permanent intracardiac pacemaker.

Patients with the bradycardia-tachycardia syndrome may be symptomatic because of either pronounced sinus slowing or arrest or rapid supraventricular arrhythmias. In the latter group, digitalis is the mainstay of therapy. Others, however, have reported further sinus node slowing after digitalis[25,37] therapy. The use of suppressants (quinidine, procaine amide, and propropanolol [Inderal®]) should be used with caution since they may result in further severe slowing of the sinus rate.[10,38] We believe that exercise stress testing (especially in young patients) is of value in uncovering serious cardiac arrhythmia, and it may suggest either restrictions of extreme exercise or more aggressive medical treatment or both. Pacemaker therapy has greatly simplified management of these patients in that the bradycardia is controlled and digitalis or suppressants or both may be used for control of supraventricular arrhythmias. In our experience, the supraventricular tachyarrhythmias in these patients were usually initiated by a premature atrial discharge (rather than escape of another supraventricular focus). Similarly, electrically induced coupled atrial premature beats regularly initiated supraventricular tachycardia in two patients in this group with evidence suggesting a sinus node reentrant arrhythmia[39] in one and A-V node reentry in the other.[40] The widespread pathologic changes already alluded to appear to present the proper milieu for these reentrant arrhythmias. Atrial overdrive pacing (or ventricular pacing with 1:1 retrograde A-V conduction) may be sufficient to prevent the supraventricular tachyarrhythmias.

Atrial demand pacemakers have the advantage over other pacemakers of preserving the normal "atrial booster" mechanism, which may be particularly important in patients with congestive heart failure. In addition, atrial overdrive may prevent supraventricular tachyarrhythmias in patients with the bradycardia-tachycardia syndrome. On the other hand, consistent pacing from either the atrium or coronary sinus may be impossible using the transvenous route of catheter insertion and may require thoracotomy with insertion of the electrodes into the atrial myocardium. Pervenous permanent right ventricular pacing is favored because of ease of catheter insertion and because the patient is protected should A-V block eventually develop. His bundle recordings and atrial pacing are quite helpful in detecting patients with associated impairment of A-V conduction who clearly require a ventricular pacemaker. Right ventricular pacing does, however, produce asynchrony between atrial and ventricular contraction, which may result in diminished cardiac output.[41] In addition, if retrograde ventriculoatrial conduction is intact, conceivably retrograde atrial impulses may trigger bouts of supraventricular arrhythmias[39,40] as discussed previously.

Finally, an experimental bifocal electrode demand pacemaker with one pacemaker positioned in the right atrium and the second in the right ventricle is also available. When sinus slowing is associated with A-V block, both atrium and ventricle are paced in sequence. This pacemaker system has been employed successfully in a relatively small number of patients with sinus node disease.[42]

Insertion of a temporary transvenous cardiac pacemaker is recommended before insertion of the permanent pacemaker to allow for a smoother intraoperative course. In addition, when appropriate, the patient may be exercised with the temporary pacemaker in place at varying paced rates to determine the rate that results in optimal cardiac performance.

REFERENCES

1. James TN: Anatomy of the human sinus node. Anat Rec 141:109-139, 1961
2. James TN, Sherf L, Fine G, et al: Comparative ultrastructure of the sinus node in man and dog. Circulation 34:139-163, 1966
3. Strauss HC, Bigger JT, Jr: Electrophysiological properties of the rabbit sinoatrial perinodal fibers. Circ Res 31:490-506, 1972
4. Kaplan BM, Langendorf R, Lev M, Pick A: Tachycardia-bradycardia syndrome (so-called "sick sinus syndrome"). Am J Cardiol 31:497-508, 1973
5. Rasmussen K: Chronic sinoatrial heart block. Am Heart J 81:38-47, 1971
6. James TN: Myocardial infarction and atrial arrhythmias. Circulation 24:761-776, 1961
7. Hudson REB: The human pacemaker and its pathology. Br Heart J 22:153-167, 1960
8. Narula OS: Atrioventricular conduction defects in patients with sinus bradycardia. Circulation 44:1096-1110, 1971
9. Rosen KM, Rahimtoola SH, Gunnar RM, et al: Transient and persistent atrial standstill with His bundle lesions. Circulation 44:220-236, 1971
10. Rubenstein JJ, Schulman CL, Yurchak PM, et al: Clinical spectrum of the sick sinus syndrome. Circulation 46:5-13, 1972
11. Conde CA, Leppo J, Lipski J, et al: Effectiveness of pacemaker treatment in the bradycardia-tachycardia syndrome. Am J Cardiol 32:209-214, 1973
12. Easley RM, Goldstein S: Sino-atrial syncope. Am J Med 50:166-177, 1971
13. Chokshi DS, Mascarenhas E, Samet P, et al: Treatment of sinoatrial rhythm disturbances with permanent cardiac pacing. Am J Cardiol 32:215-220, 1973
14. Rosen KM, Loeb HS, Sinno MZ, et al: Cardiac conduction in patients with symptomatic sinus node disease. Circulation 43: 836-844, 1971
15. Mandel WJ, Hayakawa H, Allen HN, et al: Assessment of sinus node function in patients with the sick sinus syndrome. Circulation 46:761-769, 1972
16. Ferrer MI: The sick sinus syndrome. Circulation 47:635-641, 1973
17. Fowler NO, Fenton JC, Conway GF: Syncope and cerebral dysfunction caused by bradycardia without atrioventricular block. Am Heart J 80:303-312, 1970
18. James TN, Froggatt P, Marshall TK: Sudden death in young athletes. Ann Intern Med 67:1013-1021, 1967
19. Astrand I: Aerobic work capacity in men and women with specific reference to age. Acta Physiol Scand 49(Suppl 169):1-92, 1960
20. Agruss NS, Rosin EY, Adolph RJ, et al: Significance of chronic sinus bradycardia in elderly people. Circulation 46:924-930, 1972
21. Levin AB: A simple test of cardiac function based upon the heart rate changes induced by the Valsalva maneuver. Am J Cardiol 18:90-99, 1966
22. Linenthal AJ: Effects of carotid sinus reflex on cardiac impulse formation and conduction. Circulation 20:595-601, 1959
23. Abelmann WH, Fareeduddin K: Increased tolerance of orthostatic stress in patients with heart disease. Am J Cardiol 23: 354-363, 1969
24. Orkin LR, Bergman PS, Nathanson M: Effects of atropine, scopolamine and meperidine on man. Anesthesiology 17:30-37, 1956.
25. Wan SH, Lee GS, Toh CCS: The sick sinus syndrome—A study of 15 cases. Br Heart J 34:942-952, 1972
26. Sigurd B, Jensen G, Meibom J, et al: Adams-Stokes syndrome caused by sinoatrial block. Br Heart J 35:1002-1008, 1973
27. Epstein SE, Beiser GD, Stampfer M, et al: Characterization of the circulatory response to maximal upright exercise in normal subjects and patients with heart disease. Circulation 35:1049-1062, 1967.
28. Andersen KL, Shephard RJ, Denolin H, et al: Fundamentals of Exercise Testing. Geneva, World Health Organization, 1971, pp 83-85
29. Donald DE, Shepherd JT: Response to exercise in dogs with cardiac denervation. Am J Physiol 205:393-400, 1963
30. Thomson PD: Autonomic insufficiency—Medical Staff Conference. Calif Med 113:27-34, Aug 1970
31. Narula OS, Samet P, Javier RP: Significance of the sinus-node recovery time. Circulation 45:140-158, 1972
32. Strauss HC, Saroff AL, Bigger JT Jr, et al: Premature atrial stimulation as a key to the understanding of sinoatrial conduction in man. Circulation 47:86-93, 1973
33. Mendez C, Gruhzit CC, Moe GK: Influence of cycle length upon refractory periods of auricles, ventricles and A-V node in the dog. Am J Physiol 184:287-295, 1956
34. Scherlag BJ, Lau SH, Helfant RH, et al: Catheter technique for recording His bundle activity in man. Circulation 39:13-18, 1969
35. Denes P, Delon W, Dhingra R, et al: The effects of cycle length on cardiac refractory periods in man. Circulation 49:32-41, 1974
36. Damato AN, Lau SH, Helfant RH, et al: Study of atrioventricular conduction in man using electrode catheter recordings of His bundle activity. Circulation 39:287-296, 1969
37. Short DS: The syndrome of alternating bradycardia and tachycardia. Br Heart J 16:208-214, 1954
38. Scheinman MM, Weiss AN, Shafton E, et al: Electrophysiologic effects of procaine amide in patients with intraventricular conduction delay. Circulation 49:522-529, 1974
39. Paulay KL, Varghese PJ, Damato AN: Atrial rhythms in response to an early atrial premature depolarization in man. Am Heart J 85:323-331, 1973
40. Goldreyer BN, Bigger JT Jr: Site of reentry in paroxysmal supraventricular tachycardia in man. Circulation 43:15-26, 1971
41. McNally EM, Benchimol A: Medical and physiological considerations in the use of artificial cardiac pacing—Part I. Am Heart J 75:380-398, 1968
42. Castillo CA, Castellanos A Jr, Callard G, et al: Bifocal demand pacing. Chest 59:360-364, 1971