ELECTROPHYSIOLOGIC MANIFESTATIONS IN SO-CALLED "SICK SINUS SYNDROME"

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Electrophysiologic disorders in 17 patients with sick sinus syndrome (SSS) were assessed by recording of intracardiac electrograms, atrial overdrive pacing and extrastimulus technique. Significant suppression of the sinoatrial node (SAN) by overdrive pacing (maximum corrected SAN recovery time of longer than 560 msec) was noted in 14 of 16 patients studied. In nine patients, scanning with atrial extrastimuli, sinus rest was defined in all. In one patient there was a longer interpolation zone. Calculated sinoatrial conduction time (SACT) in individual patients varied considerably. The mean SACT was over 110 msec in 5 of 9 patients (56%). Sinus echo was demonstrated in 3; one manifested SAN re-entrant tachycardia with rates of 72 to 77 beats/min. AV nodal echo was demonstrated in 3, two of them manifested AV nodal re-entrant tachycardia. Intracardiac electrograms revealed prolonged AV conduction time in 2 of 15 patients and prolonged His-Purkinje system conduction time in 2 of 17 patients studied. Two patients disclosed what we thought to be manifestation of intraatrial conduction disturbance. Both had considerable time interval between pacing impulse and atrial response. In one of them Mobitz type 1 and 2:1 intraatrial blocks were observed on atrial pacing and a possible internodal tract depolarization was also recorded. It is concluded that the electrophysiologic manifestations of patients with SSS cover a wide spectrum. The mechanism of tachycardia can be due to either SAN or AV nodal re-entry.

DURING the past several years, sinoatrial node (SAN) function and cardiac conduction in patients with sick sinus syndrome (SSS) have been extensively investigated by intracardiac electrode recording, together with pacing studies.¹⁻¹³ Nevertheless, the overall electrophysiologic manifestations of the SSS, especially of intraatrial electrical disorders and mechanism of tachyarrhythmias, are still of interest and remain to be further

clarified. The purpose of this study is to assess electrophysiologic disorders of the SSS by means of electrode recording of intracardiac electrograms in combination with atrial overdrive pacing and extrastimulus technique. SAN function, cardiac conduction, refractory period of the conducting tissues and mechanism of paroxysmal supraventricular tachycardia (PSVT) were investigated and a variety of electrophysiologic manifestations were observed.

Key Words:

Sick sinus syndrome
Re-entrant tachycardia
Intraatrial conduction disturbance
Internodal tract depolarization

MATERIALS AND METHODS

A total of 17 patients were studied, all of whom had clinical evidence for SAN dysfunction

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TABLE I CLINICAL AND ECG DATA ON 17 PATIENTS WITH THE SICK SINUS SYNDROME

Case No	Age (yr)	Sex	Etiology or additional disease	ECG Findings					Symptoms
				Arrhythmias prior to study	Heart rate* (beats/min)	P-R (sec)	QRS (sec)	Other	
1	70	M	ASCVD	SB, SAB, SA, JE, PAT	46-50	0.32	0.09	LAD	Syncope, dizzy spell, palpitation
2	69	F	ASCVD	NSR, SA, JR, PAF	46-80	0.24	0.10	—	Syncope, seizure, palpitation
3	65	F	ASCVD	SB, SAB, SA, JE	38-41	0.18	0.08	—	Syncope, seizure
4	76	M	HCVD	SB	40-50	0.20	0.08	LAD	Dizzy spell, weakness
5	32	F	U	SB, SAB, NSR	39-73	0.14	0.06	—	Dizzy spell
6	50	M	U	SB, SA, JE, NSR	40-70	0.18	0.08	—	Dizzy spell, palpitation
7	33	M	PCM	SB, SA, JE, NSR, PAF	40-65	0.14	0.06	RAD	Syncope, dizzy spell, palpitation
8	48	F	U	SB, SA, JE, NSR, PAT	45-68	0.16	0.06	—	Syncope, palpitation
9	46	F	TT, treated	SB, JR (AV dissoc)	35-43	—	0.08	—	Weakness
10	51	M	HCVD	SB, PAF	50-55	0.18	0.08	—	Weakness, palpitation
11	56	F	TT, treated	SB, SA, JE, JR, NSR, PAT	30-65	0.14	0.08	—	Syncope, dizzy spell, palpitation
12	58	M	U	SB, SA, JE, PAT	38-43	0.14	0.10	—	Syncope, dizzy spell, palpitation
13	35	M	U	SB	50-54	0.18	0.08	—	None
14	58	M	HCVD	SB, NSR, PAF	48-72	0.20	0.09	LAD	Palpitation
15	65	F	ASCVD	SB, SA, JE	39-41	0.18	0.08	LAD	Dizzy spell
16	55	M	RHD, AR, MS, mild	SB	35-37	0.20	0.08	—	Palpitation
17	58	M	U	NSR, SAB, PAT, PAF	63-71	0.16	0.08	—	Palpitation

*Heart rate in no tachyarrhythmias

Abbreviations: ASCVD = arteriosclerotic cardiovascular disease; HCVD = hypertensive cardiovascular disease; U = none or unknown; TT = thyrotoxicosis; RHD = rheumatic heart disease; AR = aortic regurgitation; MS = mitral stenosis; PCM = primary cardiomyopathy; SB = sinus bradycardia; SAB = sinoatrial block; SA = sinus arrest; JE = AV junctional escape; JR = AV junctional rhythm; NSR = normal rhythm; RAT = paroxysmal atrial tachycardia; PAF = paroxysmal atrial fibrillation; LAD = left axis deviation; RAD = right axis deviation; yr = year; min = minute; sec = second; M = male; F = female; dissoc = dissociation.

with bradyarrhythmias. They were 10 men and 7 women, ranging in ages from 32 to 76 years. The salient clinical and electrocardiographic (ECG) features of the patients are presented in Table I. Seven patients had a history of syncopal attacks and necessitated permanent pacemaker implantation. Nine patients had paroxysms of supraventricular tachyarrhythmias (5 with atrial

fibrillation and 5 with SVT). In no patients were the bradyarrhythmias related to drugs.

Electrophysiologic study was performed in the resting nonsedated postabsorptive state. Informed consent was obtained in every patient. Under fluoroscopic control, two #6F bipolar pacing electrode catheters (each with ring electrodes, 2 mm wide and 10 mm apart) were in-

TABLE II RESULT OF OVERDRIVE ATRIAL PACING IN 15 PATIENTS

Number of Patient	Control SAC (msec)	Maximum Pause (msec)	Max. Pause/Cont. SAC $\times 100$ (per cent)	Corrected SANRT (msec)
14*	707–1380 (1097 $\pm$ 190)	1316–3683 (2308 $\pm$ 636)	156–324 (211 $\pm$ 50)	565–2548 (1213 $\pm$ 569)
1#	805	1092	136	287

*Significant overdrive suppression of the sinoatrial node was observed in these patients.

#This patient had sinus bradycardia, sinoatrial block or sinus arrest and junctional escapes, and paroxysmal supraventricular tachycardia before the study. The patient was, however, noted to have normal sinus rhythm and rate at the time of study. SAC = sinus atrial cycle, msec = millisecond, Max. = maximum, Cont. = control, SANRT = sinoatrial node recovery time.

serted via the right arm vein or veins, together or separately. A pair of electrodes was positioned along the lateral wall of the right atrium slightly caudal to the region of the SAN for stimulation purposes. Another pair of electrodes of the other catheter, used to record the high right atrial electrogram (HRAE), was positioned about 1.5 cm above the other one (almost at the junction of the superior vena cava and right atrium). Still another similar bipolar catheter was inserted via the right femoral vein and positioned across the tricuspid valve for the recording of His bundle electrogram (HBE).¹⁴ Two standard ECGs (leads I and III) were simultaneously recorded using an 8-channel oscilloscopic photographic recorder (Electronics for Medicine, DR-8). Bipolar electrograms were filtered at 40–500 HZ and all recordings were made at paper speeds at 100–200 mm/sec. HBE was recorded in all 17 patients. Premature atrial beats (PABs) were introduced via the stimulating electrode pair during spontaneous sinus rhythm (SSR) by stimuli, 2 msec in duration and twice the diastolic threshold.¹² The atrial electrogram was used to trigger a programmable stimulator (R wave-coupled pulse generator, Model 5827, Medtronic Inc.). The PABs were introduced after every 12th sinus atrial cycle. The atrial cycle was scanned beginning at prematurity equivalent to approximately 80 percent of the cycle by the placement of progressively more premature beats at 10 msec decrements until the atrial effective refractory period (AERP) was reached.¹⁵ This study was carried out in 10 patients (cases 8, 9, 10, 11, 12, 13, 14, 15, 16, 17) with one failure (case 9) in whom there was AV junctional dissociation and extremely slow sinus activities. In 3 of the 9 patients (cases 13, 15, 17), the study was repeated after administration of atropine (1.0 mg iv). In

3 other patients, not included in the above, scanning with PABs was also performed during SSR. These 3 patients did not have SAN disease and also had a normal ECG.

The following measurements were made in milliseconds (msec).

1) HRAE

HRA1-HRA1: The duration of the spontaneous atrial cycle during sinus rhythm.

HRA1-S: The interval between the spontaneous atrial deflection (HRA1) of the last sinus beat and the pacing impulse (S).

S-HRA2: The interval between the pacing impulse (S) and the premature atrial deflection (HRA2) (latency).

HRA1-HRA2: The interval between the preceding sinus atrial deflection (HRA1) and the premature atrial deflection (HRA2).

HRA2-HRA3: The interval between the premature atrial deflection (HRA2) and the first post-extrasystolic atrial deflection (HRA3).

2) HBE

Corresponding intervals to those in the HRAE were measured and designated as A1, A2 and A3 instead of HRA1, HRA2 and HRA3. A–H, H–V, H1–H2 and V1–V2 intervals were defined and measured as described previously.¹⁶

Zones of sinus reset, interpolation and echoes were quantitated and sinoatrial conduction time (SACT) was calculated during the sinus reset responses as reported by Strauss and his associates⁹ and Dhingra et al.¹⁵ Zones were defined in terms of their longest and shortest HRA1–HRA2 coupling interval. For data comparison despite differences in preceding sinus atrial cycle length (HRA1–HRA1), the HRA1–HRA2 and HRA2–HRA3 were then expressed as a percentage of the immediately preceding HRA1–HRA1.⁹ Determination of refractory periods of the various con-

TABLE III SINOATRIAL NODAL RESPONSES TO ATRIAL EXTRASTIMULI

I. NORMAL CONTROL

Case No.	CL, msec Range (mean $\pm$ SD)	SACT, msec Range (mean $\pm$ SD)	Interference zone Range (% of CL)	Reset zone ⁺ Range (% of CL)	Interpolation zone Range (% of CL)	SA echo zone Range (% of CL)	AVN echo zone Range (% of CL)
1	645-744 (700 $\pm$ 28)	37-75 (54 $\pm$ 12)	—	0.31-0.78 (47)	0.35-0.37 (2)	—	—
2	816-969 (908 $\pm$ 41)	34-97 (62 $\pm$ 18)	—	0.32-0.80 (48)	0.32-0.43 (11)	0.43	—
3	798-908 (860 $\pm$ 30)	33-97 (72 $\pm$ 20)	0.85-0.98 (14)	0.42-0.82 (40)	0.30-0.40 (10)	0.39	—
II. SICK SINUS SYMPTOM							
8	842-876 (822 $\pm$ 83)	109-174 (129 $\pm$ 30)	—	0.42-0.77 (35)	—	—	0.36-0.39 (3) (AVN reentrant tachycardia)
10	979-1334 (1063 $\pm$ 70)	46-115 (91 $\pm$ 25)	—	0.38-0.72 (34)	0.39-0.45 (6)	0.31-0.40 (9) (SA reentrant tachycardia)	—
11	912-984 (936 $\pm$ 56)	100-134 (118 $\pm$ 13)	—	0.44-0.75 (31)	—	—	0.35-0.42 (7) (AVN reentrant tachycardia)
12	1270-1334 (1300 $\pm$ 281)	5-142 (79 $\pm$ 45)	0.70-0.98 (28)	0.49-0.75 (26)	—	—	—
13	989-1212 (1132 $\pm$ 46)	37-96 (69 $\pm$ 16)	—	0.30-0.70 (40)	0.29-0.32 (3)	0.36	—
*731-780 (758 $\pm$ 18)	49-68 (58 $\pm$ 8)	—	—	0.45-0.82 (37)	—	—	—
14	979-1142 (1089 $\pm$ 45)	16-224 (113 $\pm$ 67)	—	0.36-0.80 (44)	0.32-0.42 (10)	—	—
15	1035-1175 (1131 $\pm$ 42)	171-188 (180 $\pm$ 9)	—	0.39-0.44 (5)	0.40-0.60 (20)	0.38	0.33-0.37 (4)
*778-847 (812 $\pm$ 17)	84-160 (138 $\pm$ 31)	—	—	0.48-0.68 (20)	—	—	0.40-0.47 (7)
16	780-1158 (916 $\pm$ 128)	115-268 (180 $\pm$ 63)	0.80-0.98 (18)	0.35-0.79 (44)	—	—	—
17	#842-984 (933 $\pm$ 35)	52-177 (76 $\pm$ 24)	—	0.30-0.78 (48)	—	—	—
*788-1005 (896 $\pm$ 90)	18-179 (79 $\pm$ 44)	—	—	0.31-0.81 (50)	—	—	—

*Data following atropine (1 mg iv) administration.

#A short period of atrial fibrillation developed by extrastimulus at a couple interval of 30% of the cycle length before atropine administration.

+ In majority of the cases, the stimulation was begun at prematurity, equivalent to approximately 80 percent of the sinus cycle. Therefore the reset zone was probably slightly longer than that given.

Abbreviations: CL = preceding cycle length; SACT = sinoatrial conduction time; msec = millisecond; SA = sinoatrial; AVN = AV nodal.

ducting tissues was similar to that described by Wu et al¹⁷

Atrial overdrive pacing was performed in 16 out of the 17 patients using another battery-operated pacemaker (Nihon Kohden, MDP-2). One patient developed auricular flutter with slow junctional rhythm (JR) during the study and no overdrive pacing could be accomplished. The pacing pause time (or SAN recovery time) is the interval, in msec, between the last post-extrasystolic atrial deflection and the atrial deflection of the first sinus beat^{5,6}. Corrected SAN recovery time is defined as the recovery interval in excess of the preceding sinus atrial cycle length⁷. The diagnosis of sinus node reentrance and AV nodal reentrance follows the criteria described by Wu and Denes¹⁸.

RESULTS

SAN function and SA conduction in SSS

Significant suppression of the SAN by atrial overdrive pacing was noted in 14 out of 16 patients studied. The results of 15 patients are shown in Table II. All but one patient (case 1) disclosed the maximum corrected SAN recovery time longer than 560 msec (range 565–2548 msec). The case 1, a patient with sinus bradycardia (SB), SA block, or sinus arrest with junctional escape, and PSVT, had syncope, dizzy spells or palpitations for 14 years. He disclosed maximum corrected SAN recovery time of only 287 msec (130/min for 3 minutes). The control sinus atrial cycle length at the time of study was 805 msec. Atrial overdrive pacing in another patient (case 9), presented with AV dissociation and sinus arrhythmia of extremely slow rates at the time of the study, will be described later. SAN function as well as SA conduction was further investigated by SAN responses to atrial extrastimuli during SSR. Twelve patients were the subjects of this study, 9 with SAN disease and 3 without. In 3 patients with altered SAN function, this study was repeated following administration of atropine (1 mg iv). The results are summarized in Table III. In the patients with SAN disease, sinus reset was defined in all 9, while zone of interpolation was defined in 4. The zone of interpolation failed to be defined in 2 patients (cases 8, 11) because AV nodal re-entry became manifest within the range of the coupling intervals. There was a patient (case 15) who demonstrated longer zone of interpolation (20% of cycle length) than others (3–10% of cycle length) although the absolute reset and interpla-

tion zones in this patient were probably longer. This patient, however, had significant SAN suppression to overdrive pacing at a rate of 130 beats/min (maximum corrected SAN recovery time 1282 msec). Atropine administration resulted in almost no change in the corrected SAN recovery time (1200 msec) but the interpolation zone was no longer demonstrated. Sinus echo was manifested in 3 patients and AV nodal echo was demonstrated in 3. The mean values of SACT, calculated during sinus reset responses in 3 patients without SAN disease, ranged from 54 ± 12 to 72 ± 20 msec. In the individual patients with SSS, the SACT generally varied considerably as happened in 3 patients without SAN disease. The mean SACTs in these 9 patients ranged from 69 ± 16 to 180 ± 63 msec. The mean SACT was over 110 msec in 5 (cases 8, 11, 14, 15, 16) of the 9 patients with SAN disease. Significant shortening of the SACT following atropine administration was observed in only one (case 15) of the 3 patients studied ($P < 0.02$). Other conduction disturbances in SSS

There was one patient (case 12) who disclosed what we thought to be manifestations of intra-atrial conduction abnormality, along with recording of a possible internodal tract depolarization. The basic rhythm at the time of the study in this case was SB (sinus atrial cycle length 1270–1334 msec) with occasional sinus arrest and junctional escapes. The AERP was 488 msec at cycle length 1300 ± 281 msec. As shown in Fig. 1A, two separated high-frequency potentials (a, b), 95 msec apart, were recorded in HRAE during SSR, together with inverted P waves in lead III ECG (P–R interval 0.13 sec). The onsets of P waves, atrial deflections in both HRAE and HBE (HRA1 and A1) were simultaneous. A programmed premature atrial stimulation (HRA1-S= 590 msec) resulted in PAB which also demonstrated two atrial deflections, a' and b', with the latter more pronounced than that of non-paced beats (Fig. 1B). The second high-frequency potential, b', followed the a' by 95 msec and the a' preceded the low atrial electrogram (A2) by 25 msec. The P wave (P') morphology became more or less biphasic (positive-negative configuration) but with the same P–R interval as the non-paced beats. There was a considerable time interval between the stimulus (S) and onset of the HRAE (S-HRA2= 95 msec). Atrial pacing at a rate of 96 beats/min resulted in progressive lengthening of the intervals between the pacing impulse (PI) and the recorded onset of atrial depolarizations

Fig. 1. Case 2. A patient with a manifestation of intra-atrial conduction defect with recording of a possible internodal tract depolarization.

High right electrogram (HRA), His bundle electrogram (HBE) and two leads electrocardiogram (L-I, L-III) were simultaneously recorded. A pair of electrodes was positioned along the lateral wall of the right atrium slightly caudal to the region of the sinoatrial node for stimulation purposes. Another pair of electrodes of the other catheter, used to record the HRA, was positioned about 1.5cm above the former one (almost at the junction of the superior vena cava and right atrium). The atrial effective refractory period was 488msec.

A. Two high-frequency potentials (a and b), 95 msec apart, were recorded in HRA during the spontaneous sinus beats. Since the P wave (P) in lead III ECG was inverted ($P-R=0.13$ sec), and the onsets of P and atrial deflections in both HRA and HBE (HRA1 and A1) were simultaneous, the basic rhythm in non-paced beats was probably mid-atrial or low-atrial in origin. The premature atrial beat (third beat) induced by an extrastimulus (S) (HRA1-S=590msec) also disclosed two atrial potentials (a' and b'),

95msec apart, and the P wave (P') morphology became more or less biphasic (positive-negative configuration) but with the same P-R interval as the non-paced beats. The a' preceded the low atrial electrogram (A2) by 25msec and the b' became more conspicuous than b. There was a considerable latency between the S and onset of the HRA2 (95msec). This considerable latency was observed by programmed premature atrial stimuli with HRA1-S ranging from 500 to 750msec and neither repetitive atrial firing nor atrial fibrillation was demonstrated. Therefore, the prolonged S-HRA2 was considered to be due to intraatrial conduction defect (first degree intraatrial block)—conduction disturbance between pacing site and recording sites (high right atrium and low atrium near the septum). The second high frequency potential (b, b') of both non-paced and paced beat was a probable internodal tract depolarization.

B. Progressive lengthening of the latency (90, 105, 120msec) with subsequent block (Mobitz type I intraatrial block) was noted with atrial pacing at a rate of 96 beats/min. The P wave was clearly biphasic in configuration. Two high-frequency potentials (a' and b'), 87 to 107 msec apart, were also noted. Since conduction to both recording sites was blocked simultaneously, the pathological lesion might have been located around the pacing site.

C. Increase in the atrial pacing rate (119 beats/min) resulted in more prolonged latency (110 msec) and 2:1 block (second degree intraatrial block).

in both HRAE (PI-HRA) and HBE (PI-A) with subsequent block (Fig. 1B). The P waves in lead III ECG were still more or less biphasic and two high-frequency potentials remained to be observed. The AV nodal and His-Purkinje system (HPS) conduction times were within normal limits. Further increase in the pacing rate (119 beats/min) caused more pronounced increase in the PI-HRA intervals and 2:1 block (Fig. 1C). Prolongation of the interval between PI and the recorded onset of atrial depolarization in HRAE was observed in another patient (case 9) with AV junctional dissociation and extremely slow sinus beats. The PI-HRA interval was 26 msec at a pacing rate 80 beats/min (Fig. 2B). The interval increased to 89 msec at a pacing rate 100 beats/min and the atrial deflections in HRAE were not uniform from time to time (Fig. 2C). The lower atrial depolarization (A) preceded high atrial depolarization (HRA) by 37 msec. The P waves in paced beats were upright in lead III ECG at the pacing rate 80 beats/min but were biphasic in

Fig. 2. Case 9. A patient with AV dissociation and extremely slow sinus mechanism.

HBE, HRA and two leads ECG (L-I, L-III) were simultaneously recorded.

A. Control rhythm tracing

Extremely slow sinus mechanism with sinus arrhythmia and AV dissociation were noted before pacing study. Sinus atrial cycle length (HRA-HRA) varied from 1590 to over 1850 msec (it ranged from 1460 to 1960, 1785 ± 65 msec when all control cycles were taken into account). AV junctional beat was rather stable with relatively constant cycle length (H-H) except occasional premature AV junctional beats. The H-H interval ranged from 1425 to 1470 msec (it was from 1360 to 1470, 1410 ± 25 msec during the study). The third AV junctional beat was a premature AV junctional beat because no atrial deflection preceded His potential (H). Moreover, it was observed that in other strips the "A" in HRA had no relation to the "H" in HBE in such beats.

B. Following cessation of 3 minutes' overdrive atrial pacing (PI) at a rate of 80 beats/min, the sinoatrial node recovery time (HRA-HRA) was 2450 msec. Note that the AV junctional automaticity remained almost unchanged and AV junctional recovery time (H-H) was 1550 msec. The latency (PI-HRA) was 26 msec. The P waves in paced beats were upright.

C. Increase in the overdrive atrial pacing rate to 100 beats/min did not disclose further prolongation of either sinoatrial node recovery time or AV junctional recovery time (HRA-

HRA=2190 and H-H=1430 msec, respectively). Note also that the high atrial deflections (HRA) were not uniform from time to time. The low atrial depolarization (A) preceded the high atrial depolarization (HRA) by 37 msec. The latency (PI-HRA) was 89 msec. The P waves in paced beat became biphasic in lead III ECG and sequence of atrial depolarization seemed changed as compared to Figure B. The extremely prolonged latency is considered to be due to intraatrial conduction defect (see text. Other conduction disturbances in SSS). Atrial effective refractory period was 479 msec in this case.

the same lead ECG at the pacing rate 100 beats/min.

AV conduction was studied by HBE in 15 patients at SSR, AV junctional rhythm with auricular flutter in one, and at AV dissociation with slow sinus rates in another. AV nodal conduction time was prolonged ($A-H \geq 125$ msec) in two of 15 patients (135 and 250 msec, respectively). HPS conduction time was prolonged ($H-V \geq 55$ msec) in two of the 17 patients (58 and 60 msec, respectively). Atrial overdrive pacing at rates below 130 beats/min resulted in 2° A-V block of Mobitz type I (Wenckebach period) in 4 out of 16 patients studied. None was observed to have prolonged internodal conduction time ($HRA-A \geq 50$ msec) at SSR.

AV junctional automaticity in SSS

In one patient (case 9) with AV dissociation and sinus arrhythmia of extremely slow rates, the automaticity of the AV junctional tissue could be determined by atrial overdrive pacing. The control sinus atrial cycles (A-A) in this patient varied considerably, being from 1460 to 1960 msec (1785 ± 65). The AV junctional cycle (H-H), before the overdrive pacing, ranged from 1360 to 1470 msec (1410 ± 25). As shown in Fig. 2A, B, following 3 minutes' atrial pacing at a rate of 80 beats/min, SAN recovery time was 2450 msec. The AV junctional automaticity remained almost unchanged by the overdrive pacing. The AV junctional recovery time was 1550 msec, which almost equaled AV junctional cycles before pacing. Increase in the pacing rate up to 100 beats/min did not disclose further prolongation of either SAN recovery time or AV junctional recovery time (2190 and 1430 msec, respectively) (Fig. 2C).

Refractory periods of various conducting tissues and mechanism of PSVTs in SSS

Refractory periods of the various conducting tissues are shown in Table IV. Prolonged AERP

TABLE IV REFRACTORY PERIOD (MSEC) FOR THE CONDUCTION TISSUES
1. NORMAL CONTROL

Case No	CL	Atrium (ERP)	AVN (ERP)	Bundle of His (ERP)	Ventricle (ERP)	(RRP)	Bundle	Branch
1	700 ± 28	235	290	----	----	371	----	
2	908 ± 41	229	285	----	----	----	442	(RB)
3	860 ± 30	203	276	----	----	----	----	
2. SICK SINUS SYNDROME								
8	822 ± 83	237	280	367	----	----	----	
10	1063 ± 70	265	364	----	403	469	469	(RB)
11	936 ± 56	286	300	----	----	----	----	
12	1300 ± 281	488	†	----	----	556	556	(LB)
13	1132 ± 46	326	356	522	----	525	----	
14	1089 ± 45	311	†	----	----	500	----	
15	1131 ± 42	296	†	453	----	505	505	(RB)
	*(812 ± 17)	(267)	†	----	----	(427)	(427)	(RB)
16	916 ± 128	321	†	----	----	----	504	(RB)
17	933 ± 35	229	270	338	----	395	417	(RB)

*() After atropine 1 mg iv administration.

† Less than the atrial ERP

Abbreviation: CL = cycle length; AVN = AV node; ERP = effective refractory period; ERP = relative refractory period; RB = right bundle; LB = left bundle.

Fig.3. Case 10. A patient with the induced paroxysmal sinus re-entrant tachycardia with atrial extrastimuli.

HBE, HRA and two ECG leads (L-I, L-III) were simultaneously recorded. The stimulus (S) was coupled to sinus rhythm at a cycle length (HRA1-HRA1) of 1076 msec (top tracing) and 1329 msec (bottom tracing), respectively. The coupling interval (HRA1-HRA2) was 360 and 450 msec, respectively. Echo (E) with paroxysmal sinus re-entrant tachycardia induction is demonstrated. Note that, during the tachycardia, atrial depolarization sequence went from high to low, and the P wave morphology was similar to sinus P. The sinus rate was only 72 to 77 beats/min. Atrial effective refractory period was 265 msec in this case.

Fig.4. Case 8. A patient with the induced paroxysmal AV nodal re-entrant tachycardia with atrial extrastimulus.

HRA, HBE and two ECG leads (L-I, L-III) were simultaneously recorded. The stimulus (S) was coupled to sinus rhythm at a cycle length (HRA1-HRA1) of 860 msec. A1-A2 was 340 msec. Note that during paroxysmal AV nodal re-entrant tachycardia, atrial depolarization sequence went from low to high and P wave morphology was different from sinus P. The atrial rate during tachycardia was 142-145 beats/min.

(over 360 msec) was noted in only one patient (case 12: 488 msec) who had a mean cycle length of 1300 msec. AV nodal effective refractory periods in 5 patients observed were in normal range. The mean cycle lengths in these 5 patients were from 822 to 1132 msec and the effective

refractory period of the AV node ranged from 270 to 356 msec. Refractory periods in other conducting tissues were probably prolonged in some patients.

Reproducible episodes of atrial tachycardia were elicited by atrial extrastimulus technique in 3 of 9 patients studied. Of these, one patient (case 10) manifested SAN re-entrant tachycardia (echo zone 31–40% of the cycle length) with rates of 72 to 77 beats/min (Fig. 3). The mean control cycle length before extrastimuli was 1063 ± 70 msec in this patient. The remaining two patients (cases 8, 11) disclosed AV nodal re-entrant tachycardia (rates 142–145 and 158–160 beats/min, respectively) with echo zones 36–39% and 35–42% of the cycle length, respectively (Fig. 4). There was another patient (case 17) who developed reproducible short runs of atrial fibrillation by extrastimuli at a coupling interval of 30% of the cycle length.

DISCUSSION

The pathologic electrophysiologic mechanisms of the sinoatrial dysrhythmias observed in the SSS have been postulated as: 1) abnormalities of the SAN as an electric generator; 2) abnormalities of conduction from the SAN to the atrium; and 3) atrial nonresponsiveness due to subthreshold sinus impulse.^{3,4,19–21} However, it seems that some simultaneous lesions in other parts of the heart are not uncommon in symptomatic SAN disease^{1,2,20,22,23} and a new term "panconductional defect"²² has been proposed for this particular entity.

Evaluation of SAN function, both in normal subjects and patients with SSS, has attracted increasing interest over the past years. Extensive studies have been performed using various methods including atrial overdrive pacing^{5–7} and extrastimulus technique^{9–13,15,19}. The determination of SAN recovery time after atrial overdrive pacing has been said to be the most sensitive method for the detection of SAN dysfunction by some workers.²³ Yet, there have been some patients with significant SAN disease in whom normal or doubtful results are observed.⁶ For this method to be valid, there should be no delay or block in conduction between the atrium and SAN even though atrial discharge remains regular on the atrial pacing.⁹ One of our patients was an example of this. This patient had had spontaneous paroxysmal SA block or sinus arrest together with PSVT of 14 years' duration, yet the maximum SAN recovery time was 1092 msec

(maximum corrected SAN recovery time 287 msec) after 3 minutes' atrial pacing at a rate of 130 beats/min (preceding sinus cycle 805 msec). Programmed premature atrial depolarization, along with calculation of SACT has recently been advocated for evaluation of the SAN disease by Strauss et al.⁹ The sum of retrograde and antegrade SA conduction time has been considered to be prolonged if it exceeds 215 msec.¹⁰ In our 9 patients studied, only 5 had the mean conduction time (the difference between return cycle during reset and spontaneous sinus cycle, divided by 2) over 110 msec and 3 exceeded 120 msec. Moreover, in these patients and those with normal SAN function, the calculated conduction time varied considerably in the same patient within the reset zone. It is of note that in one of our patients there was an increase in the interpolation zone and sinus reset was rather difficult to obtain by induced extrastimuli. In the series of Strauss et al.⁹ reset was never observed in one of 5 patients with SAN dysfunction. They have considered the fact that the atrial premature depolarization never reset the SAN is due to first degree SA block with interference. In our patient, however, significant suppression of the SAN was noted by atrial overdrive pacing at a rate of 130 beats/min. The reset response became easy to obtain and significant shortening of SACT was also observed after administration of atropine. Atropine administration has been reported to shorten the SACT¹³ but this was not the case in two other patients studied. Evaluation of SACT in the diagnosis of SAN dysfunction has recently been criticized by Reiffel et al.¹² together with Breithardt and his associate.¹¹ The value obtained can vary considerably in the presence of sinus arrhythmia and also in relation to changes in return cycle following an APD. A shortened return cycle has been known to occur as a result of either early PASS²⁵ or long preceding sinus atrial cycle length.²⁶ The premature depolarization of the sinus node may also have a depressant effect on sinus node automaticity and thus overestimation of true SACT can occur.¹¹ In the present series we also observed considerable variation in the calculated values in the same patient when the whole reset zone was scanned. However, the mean SACT was prolonged (over 110 msec) in 5 out of 9 patients (56%), the percentage being greater than that reported by Strauss et al (38%).¹⁰ Among electrophysiologic disorders, other than impaired SAN automaticity and SA conduction disturbance in the SSS, intra-

atrial conduction defect is of interest.

Despite the numerous descriptions of electrophysiologic manifestations in patients with SSS, there have been only a few reports dealing with intraatrial conduction defect in this group of patients available.^{2,4} Such information could be expected to enhance further our understanding of the underlying electrophysiologic mechanisms as well as give us an overview of the disease process. Rosen et al⁴ described electrophysiologic manifestations together with histologic correlations of a patient in whom the SA block appeared to reflect involvement of the SAN approaches. A high-frequency potential preceding the onset of both a P wave and a local bipolar electrogram was recorded in this patient and they considered this to be posterior internodal tract depolarization. Intraatrial conduction delay (P-A time ranged from 55 to 120 msec) was noted in 10 of 50 patients with sinus bradycardia by Narula.² In the present series, there was one patient who had what we thought to be manifestations of intraatrial conduction defect, together with recording of a certain kind of internodal tract depolarization. This patient disclosed two separate high-frequency potentials in the HRAE of both non-paced and paced beats. As P wave was inverted in lead III ECG, and onsets of P wave, atrial deflections in both HRAE and HBE were simultaneous, the basic rhythm in non-paced beat was probably mid-atrial or low atrial in origin. On atrial pacing with electrode catheter tip positioned at about 1.5 cm caudal to the right atrium-SAN junction, there was considerable time interval between pacing impulse and onset of atrial deflection in either HRAE (electrode catheter tip being located at the right atrium-SAN junction) or HBE. The P wave in lead III ECG became biphasic (positive-negative configuration) in the paced beats. The interval between pacing impulse and atrial deflection was quite prolonged in this patient. Pacing of a structure or chamber may produce a latency period between the stimulus and the recorded onset of depolarization in the structure being paced. This latency period has been observed in a range of 15 to 20 msec on atrial pacing for 15 normal subjects. Stimulation during the atrial relative refractory period ("vulnerable period") has been demonstrated to cause increased latency between pacing impulse and response, together with prolonged intraatrial conduction.^{19,27} Repetitive atrial firing or atrial fibrillation may follow in such a situation.¹⁹ In our patient, although the

AERP was prolonged (488 msec), considerable latency was observed by programmed premature atrial stimuli (HRA1-S= 500–750 msec) and neither repetitive atrial firing nor atrial fibrillation was demonstrated. It is, therefore, possible that the prolonged latency is not related to the extended atrial refractory period in our patient. The prolonged interval between pacing impulse and atrial response might have resulted from intraatrial conduction defect with widespread pathologic lesion involving the atrial tissue. This assumption is substantiated by atrial pacing at rates of 96 and 119 beats/min, which resulted in more advanced block (Wenckebach period and 2 : 1 intraatrial block). An alternate possibility for this increased latency is that the patient had exit block to the atrium. Shortening of atrial cycle length by pacing resulted increased conduction time or block between the atrium and the SAN, through the SAN perinodal fiber. However, this possibility is not quite likely in our patient because the pacing electrodes were not positioned at the junction of the superior vena cava and the right atrium (region of the SAN) and the SAN was not directly paced. Rosen et al⁴ stated that, in atrial conduction disease, the internodal tract and the rest of the atrium may be out of phase and internodal tract depolarization can be recorded. Thus, the second high frequency potential in HRAE in our patient may have reflected activity of a certain kind of the atrial specialized conduction system. The prolonged interval between pacing impulse and onset of atrial depolarization on pacing was also noted in another patient who had AV junctional dissociation and extremely slow sinus rates. This was only elicited at a pacing rate of 100 beats/min.

In SSS, impaired impulse formation by lower automatic centers has also been noted and from a clinical standpoint the cerebral ischemic symptom is actually related to the markedly delayed or escape mechanism ("sick escape pacemaker syndrome").²³ In one patient with AV dissociation and sinus arrhythmia of extremely slow rates, the automaticity of the AV junctional tissue could be determined by atrial overdrive pacing. It was surprising to find that the lower automatic centers had remarkably stable automaticity, without significant prolongation of the recovery time, following the overdrive pacing. This observation was compatible with the fact that this patient had no history of syncopal attack or dizzy spells. There have been no available data in man to indicate the normal escape interval of lower or sub-

sidary pacemakers following suppression of SAN by atrial overdrive pacing. In animal studies, however, a greater depression or longer recovery time of the AV junctional pacemakers than the SAN has been suggested by crushing of the SAN.²⁴

Little has been known about the mechanism of paroxysmal tachyarrhythmias in SSS. SAN reciprocation has been observed as the mechanism of episodic atrial tachycardia in one patient reported by Paritzky et al.¹³ In the present series, reproducible episodes of atrial tachycardia could be elicited by atrial extrastimulus technique in 3 patients; one was possibly due to SAN re-entry and the other two, AV nodal re-entry. It is of interest that the atrial rate in our patient with sinus re-entrant tachycardia elicited via extrastimulus technique was only 72–77 beats/min. It has been reported that pacemaker therapy with ventricular approach in isolated cases can be an adequate therapy for PSVT in the SSS.^{28,29} This has been explained by the fact that ventricular pacing can cause ventriculoatrial conduction and in this way, the retrograde excitation helps to abort junctional tachycardia or re-entrant tachycardias originating from the AV junction.³⁰ No electrophysiologic confirmation of intermittent tachyarrhythmias due to AV nodal re-entry mechanism, however, has been reported in SSS. Our present studies support the fore-going concept that the ventricular pacing can abort or prevent tachyarrhythmias in some patients with SSS and AV nodal reciprocation can be another mechanism responsible for atrial tachyarrhythmias.

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