



## Cardiovascular Responses to Vibrostimulation for Sperm Retrieval in Men With Spinal Cord Injury

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### Abstract

**Background/Objective:** Cardiovascular abnormalities and arrhythmias are common in individuals with spinal cord injury (SCI) who are undergoing vibrostimulation for sperm retrieval. The study aimed to examine cardiovascular control in men with SCI undergoing this procedure.

**Methods:** Individuals with chronic cervical ( $n = 8$ ; age:  $33.1 \pm 1.9$  years) and upper thoracic SCI ( $n = 5$ ; age:  $35.2 \pm 2.9$  years) volunteered for vibrostimulation, with continuous blood pressure (Finometer) and electrocardiographic monitoring. Patients were characterized further by sympathetic skin responses (SSR) to assess descending autonomic spinal pathways and American Spinal Injury Association (ASIA) scores to assess motor and sensory pathways.

**Results:** All but one subject with cervical SCI were ASIA A or B and were negative for SSR in the hands and feet. All subjects with upper thoracic SCI were ASIA A or B and were positive for SSR in the hands. Systolic blood pressure was lower in men with cervical injury at rest. Vibrostimulation induced an increase in systolic blood pressure  $>20$  mmHg in all patients with cervical SCI (range = 125/65–280/152; median = 167/143 mmHg) and in 2 thoracic subjects (151/104 and 170/121 mmHg). During ejaculation, 6 cervical and 3 thoracic subjects developed arrhythmias (5 with bradycardia, 6 with premature atrial contractions, 4 with ventricular excitation, 1 with junctional rhythm, and 1 with heart block).

**Conclusion:** The vibrostimulation procedure induced electrocardiographic abnormalities and autonomic dysreflexia in subjects with either cervical or high thoracic SCI.

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**Key Words:** Spinal cord injuries; Arrhythmia; Autonomic dysreflexia; Sympathetic skin response; Vibrostimulation; Sperm retrieval

### INTRODUCTION

Individuals with spinal cord injury (SCI) are reported to be at increased risk of mortality compared to able-bodied

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persons, and death among individuals with SCI is primarily due to cardiovascular causes (1). However, the reasons for this are uncertain. It may be that SCI increases the risk of unstable blood pressure and cardiac arrhythmias (2–5) or other electrocardiographic (ECG) abnormalities (6,7) that may predispose patients to adverse cardiac events. Most previous studies examining the incidence of cardiac arrhythmias in SCI patients have been performed while the subject was in the resting state (2,8,9). It is possible that the incidence of arrhythmia is increased during certain procedures or situations and, in particular, during episodes of autonomic dysreflexia (5).

Autonomic dysreflexia refers to sudden bouts of high blood pressure (defined here as an increase in systolic

blood pressure of greater than 20 mmHg) triggered by noxious or nonnoxious afferent stimuli below the level of the spinal cord lesion; autonomic dysreflexia is characterized by pounding headache and upper-body flushing (10,11). The incidences of both autonomic dysreflexia and cardiac arrhythmia are reported to be related to the level of SCI, with higher level lesions carrying the greatest risk (2,4,6,12,13). Some studies have examined a possible link between severity of SCI, as assessed by the American Spinal Injury Association (ASIA) score (14), and autonomic dysreflexia (10) or cardiac arrhythmia (1,2), but these studies have yielded inconsistent results. This is not surprising, since the ASIA score examines the motor and sensory impairment associated with the SCI and does not account for autonomic nervous system integrity (15–17), which is likely to be of greater importance in the etiology of autonomic dysreflexia or ECG abnormalities. It is to be expected that the incidence of autonomic dysreflexia would be related to the lack of integrity of sympathetic spinal autonomic reflexes (18). However, it may be that the incidence of ECG abnormalities is also related to the integrity of spinal autonomic circuits, either directly (through the presence or absence of sympathetic control of the heart) or indirectly (through the severity and frequency of episodes of autonomic dysreflexia).

The aim of this study, therefore, was to examine the incidence of blood pressure and ECG abnormalities in individuals with chronic severe SCI undergoing vibrostimulation for sperm retrieval, a procedure known to carry a risk of inducing autonomic dysreflexia (19). We hypothesized that those individuals with greater impairment of spinal autonomic pathways would be likely to experience more severe autonomic dysreflexia and a greater incidence of cardiac arrhythmia or other ECG abnormalities than those in whom these pathways were preserved.

## METHODS

### Subjects

The study was approved by the Vancouver General Hospital and University of British Columbia Research Ethics Committees and was performed in association with the Declaration of Helsinki (2002) of the World Medical Association. We performed offline analysis of data obtained from 13 men with chronic SCI, all of whom were undergoing vibrostimulation for sperm retrieval. Twelve of these subjects had participated in a previous study on the effects of sildenafil citrate on autonomic dysreflexia during sperm retrieval (20). The data in the present study were used for the determination of the incidence of cardiac arrhythmia during sperm retrieval and the examination of the potential relationship between arrhythmia and the absence of spinal autonomic pathways. All subjects were apparently healthy and taking no cardiovascular medication. None of the volunteers had any known cardiovascular disease, and all were free from pain and pressure ulcers. All subjects

gave written informed consent. Based on the ASIA assessment, volunteers were divided into 2 groups: cervical SCI ( $n = 8$ ) and thoracic SCI ( $n = 5$ ). Within each group, individuals were also classified according to completeness of injury using the ASIA assessment.

### Procedure

Studies were performed in the mornings following a light breakfast in a temperature-controlled laboratory (22–25°C). Subjects were asked to abstain from drinking alcohol from the night before the test and to abstain from drinking caffeine or smoking on the morning of the tests. On arrival at the laboratory, the ASIA assessment was performed. After a short break, during which subjects were instructed to empty their bladders, subjects had their sympathetic skin responses determined. After a second short break, subjects rested in the supine position for 10 minutes prior to the onset of the vibrostimulation procedure, during which time baseline blood pressure and ECG recordings were obtained.

*ASIA Assessment.* The ASIA/International Medical Society of Paraplegia (IMSOP) score was utilized for neurological classification of the level and severity of SCI through the assessment of the motor and sensory impairment (14). The ASIA assessment was conducted by a physician trained in the ASIA assessment protocol. ASIA grades A (motor and sensory complete) and B (motor complete) represent severe SCI, and ASIA grade C characterizes moderate SCI (motor incomplete, although nonfunctional). None of the subjects who volunteered for this study was characterized as ASIA grades D (motor incomplete, functional) or E (normal motor and sensory function).

*Sympathetic Skin Responses.* The integrity of the descending spinal autonomic pathways was assessed using sympathetic skin responses (SSR). This response examines the neural control of sympathetic cholinergic sudomotor fibers, which is dependent upon the integrity of central and peripheral sympathetic circuits (15). SSR were recorded bilaterally and simultaneously from both hands and feet using self-adhesive electrodes (sampled at a band pass of 3 Hz–3 kHz). Each stimulus consisted of a single electric pulse of 0.2-millisecond (ms) duration and an intensity of 8 to 10 milliamperes (mA). In all subjects, a standard stimulation protocol was applied, whereby subjects were stimulated at the left median nerve at the wrist and the left posterior tibial nerve at the ankle. A total of 10 stimuli were applied at each location, with variable time delays in order to eliminate habituation. Data were recorded continuously using an analog-to-digital converter (Powerlab/16SP Model ML795, AD Instruments, Colorado Springs, CO) interfaced with a computer. Data were stored for subsequent offline analysis using specialized software (Powerlab version 5.0.2, AD Instruments). Responses were quantified by the number of reproducible SSR elicited, with a normal latency and duration at each site

(15). Thus, the maximum response at each site would score 10, if all 10 stimuli elicited a normal SSR.

**Cardiovascular Assessment.** Subjects were instrumented with a standard 3-lead ECG (lead II; Powerlab Model ML132) and beat-to-beat blood pressure monitoring device (Finometer, Finapres Medical Systems BV, Arnhem, The Netherlands). Data acquisition and storage were performed using Powerlab Chart 5, version 5.0.1 (New South Wales, Australia). The cardiovascular parameters were continuously monitored and recorded throughout the vibrostimulation procedure and for an additional 10-minute recovery period following the vibrostimulation procedure. All variables measured throughout the procedure were averaged over 10-beat windows. Electrocardiographic and blood pressure analyses were performed offline after completion of the study by a “blinded” investigator certified in electrocardiography. For the purposes of this study, ECGs were classified as abnormal if they did not fulfill the criteria for “normal sinus rhythm”; thus, we included sinus bradycardia (heart rate <60 beats per minute [bpm]), sinus tachycardia (heart rate >100 bpm), and any arrhythmia. Following instrumentation, subjects then rested in the supine position for 10 minutes, during which time baseline recordings were made. We defined autonomic dysreflexia as an increase in the systolic blood pressure of 20 mmHg or greater (21).

**Vibrostimulation Procedure.** After the 10-minute rest period, either a WAHL vibrator (WAHL model 4196, Div Swenson Canada Inc, Toronto, Ontario, Canada) or Ferticare Clinic vibrator (Multicept APS, Rungsted, Denmark) was used for the vibrostimulation procedure. These specialty vibrators are capable of applying various amplitudes and speeds of vibration and were administered by a medical doctor who is an expert in clinical sperm retrieval techniques. Clinical judgment and experience of this investigator allowed for either ejaculation or cessation of the procedure if ejaculation was deemed unsuccessful or was considered unsafe. Subjects were observed throughout the investigation for the presence of symptoms or signs of autonomic dysreflexia. This method of vibrostimulation is standard in our sperm retrieval clinic and those of others (20,22–24).

**Statistical Analysis.** All statistical analyses were performed using GraphPad InStat version 3.00 for Windows 95 (GraphPad Software, San Diego, CA). Data are expressed as means  $\pm$  SEM. Values were tested for normality using the Kolmogorov and Smirnov assumptions. Comparisons between the 2 groups were performed using unpaired Student’s *t* tests. Within-group comparisons were performed using repeated-measures analysis of variance with the Dunnett or Tukey post-hoc test. Correlations between variables were performed using the Spearman ranked correlation coefficient. Comparisons between incidences of autonomic dysreflexia were examined using Fisher’s exact test.

Statistical significance was assumed at the level of  $P < 0.05$ .

## RESULTS

### Subject Characteristics

Eight subjects had sustained cervical SCI (mean age,  $33.1 \pm 1.9$  years; height,  $164.9 \pm 3.5$  cm; and weight,  $74.3 \pm 3.8$  kg), and 5 had thoracic SCI (mean age,  $35.2 \pm 2.9$  years; height,  $160.4 \pm 1.7$  cm; and weight,  $76.4 \pm 3.0$  kg). There were no significant differences in any of these parameters between the 2 groups. Sporting injuries were the predominant cause of SCI in these subjects (54%), followed by motor vehicle accidents (38%). The mean duration from injury to investigation was similar in both groups ( $140.6 \pm 26.6$  months in the cervical SCI and  $164.2 \pm 39.3$  months in the thoracic SCI group). Individual subject characteristics are shown in Table 1. The majority of subjects with cervical (63%) and thoracic (80%) injuries had sustained complete (ASIA A) SCI.

### Sympathetic Skin Responses

No SSR were obtained in response to stimulation of the posterior tibial nerves in any subject (data not shown). SSR for each subject from both palmar and plantar surfaces in response to median nerve stimulation are presented in Table 2. SSR could not be elicited from the plantar surface in any subject. In the cervical group, only 1 subject (subject 6) had asymmetrical, but preserved, palmar SSR. All subjects with thoracic SCI had intact palmar SSR in response to median nerve stimulation.

### Cardiovascular Responses to the Vibrostimulation Procedure

The cardiovascular responses to the vibrostimulation procedure can be seen in Table 3. There were no significant differences in resting RR interval, heart rate, diastolic pressure, or mean pressure between the 2 groups; however, the resting systolic blood pressure was lower in subjects with cervical SCI ( $P < 0.05$ ). During ejaculation, both groups showed increases in blood pressures that were defined as autonomic dysreflexia (increase by <20 mmHg in systolic pressure) in all individuals with cervical SCI and in 40% of those individuals with thoracic SCI (Table 2). These blood pressure increases were statistically significant only in the cervical SCI individuals, in whom the blood pressure increase was larger. The maximum recorded blood pressures during ejaculation were 280/152 mmHg in the cervical group (subject 2) and 170/121 in the thoracic group (subject 13). Bradycardia associated with ejaculation (and autonomic dysreflexia) was observed in the cervical SCI group, and a modest increase in heart rate was seen in the thoracic SCI group (not significant). During the recovery period, heart rate returned to baseline levels in both groups, and blood pressures began to return to the resting supine levels. However,

**Table 1.** Subject Characteristics\*

Subject	SCI	Age (y)	Height (cm)	Weight (kg)	Time Since SCI (mo)	Cause of SCI
1	C2 ASIA A	34	161	91	187	MVC
2	C4 ASIA A	35	161	77	194	Sport
3	C4 ASIA B	26	161	62	73	MVC
4	C4 ASIA B	29	160	84	65	Other
5	C4 ASIA B	44	172	64	285	Sport
6	C5 ASIA C	29	157	67	115	Sport
7	C6 ASIA A	34	187	82	96	MVC
8	C7 ASIA A	34	160	67	110	Sport
9	T3 ASIA A	34	166	68	99	Sport
10	T4 ASIA A	28	161	82	47	Sport
11	T5 ASIA A	37	157	82	191	MVC
12	T5 ASIA C	45	157	80	239	MVC
13	T6 ASIA A	32	161	70	257	Sport

\*Subjects were grouped according to level of injury. In one subject, the cause of SCI was “other” and was attributable to an industrial accident on a construction site. MVC, motor vehicle crash.

the blood pressures remained elevated compared with the resting data even after 10 minutes of recovery.

#### **Incidence of ECG Abnormalities During the Vibrostimulation Procedure**

The number and type of ECG abnormalities observed in each subject at the various stages of the testing procedure (rest, vibrostimulation, ejaculation, and recovery) are shown in Table 4.

*1. Arrhythmia.* Arrhythmias were common in both cervical and thoracic SCI. The most common arrhythmias noted were ventricular ectopic beats and premature atrial contractions. These were observed in isolation and as couplets or triplets, and occurred in bigeminy. In one subject, multifocal ventricular ectopic beats were observed (subject 4). One subject developed junctional bradycardia during the recovery phase (subject 1), and 2 subjects had nonconducted P waves (subjects 4 and 5). One subject had nonspecific inverted T waves

**Table 2.** Sympathetic Skin Responses (SSR) in Response to Median Nerve Stimulation and Incidence of Autonomic Dysreflexia (AD) During Vibrostimulation\*

Subject	SCI	SSR (palmar)		SSR (plantar)		Autonomic Dysreflexia/ Blood Pressure (mmHg)
		L/R	L/R	L/R	L/R	
1	C2 ASIA A	0/0	0/0	0/0	0/0	Yes (167/143)
2	C4 ASIA A	0/0	0/0	0/0	0/0	Yes (280/152)
3	C4 ASIA B	0/0	0/0	0/0	0/0	Yes (147/125)
4	C4 ASIA B	0/0	0/0	0/0	0/0	Yes (125/65)
5	C4 ASIA B	0/0	0/0	0/0	0/0	Yes (235/177)
6	C5 ASIA C	10/2	0/0	0/0	0/0	Yes (211/145)
7	C6 ASIA A	0/0	0/0	0/0	0/0	Yes (131/91)
8	C7 ASIA A	0/0	0/0	0/0	0/0	Yes (222/133)
9	T3 ASIA A	10/0	0/0	0/0	0/0	No (104/79)
10	T4 ASIA A	10/10	0/0	0/0	0/0	No (142/87)
11	T5 ASIA A	8/8	0/0	0/0	0/0	Yes (151/104)
12	T6 ASIA A	10/10	0/0	0/0	0/0	No (143/120)
13	T5 ASIA C	10/10	0/0	0/0	0/0	Yes (170/121)

\*Ten stimuli were applied to each nerve in random fashion to eliminate habituation. The number of positive SSR are indicated on the left (L) and right (R) sides of the body. The highest blood pressure reading recorded during the test is noted, and also noted is whether this is indicative of an episode of AD. Complete lesions, as identified by ASIA score, did not necessarily correlate with the absence of SSR. Individuals with a higher level of injury and absent palmar SSR were more likely to experience severe autonomic dysreflexia.

**Table 3.** Blood Pressures and Heart Rate Responses During the Vibrostimulation Procedure in Men With Cervical and Thoracic SCI\*

	RRI (ms)	HR (bpm)	SAP (mmHg)	DAP (mmHg)	MAP (mmHg)
<b>Rest</b>					
Cervical	998.3 ± 75.0	65.0 ± 5.0	82.8 ± 7.6†	54.7 ± 6.2	64.1 ± 6.6
Thoracic	912.9 ± 62.2	67.2 ± 4.3	110.9 ± 12.2	64.8 ± 7.1	79.4 ± 8.7
<b>Ejaculation</b>					
Cervical	1093.4 ± 94.7	57.1 ± 3.8	189.8 ± 19.7¶	128.9 ± 12.6¶	149.2 ± 14.1¶
Thoracic	869.6 ± 99.9	74.2 ± 11.6	142.0 ± 9.6	102.0 ± 7.6	118.3 ± 10.1
<b>Recovery</b>					
Cervical	1067.5 ± 84.8	59.8 ± 5.6	138.1 ± 13.6‡	94.7 ± 11.9	109.2 ± 12.2
Thoracic	946.3 ± 76.5	65.1 ± 6.0	139.3 ± 7.6	95.1 ± 4.5	109.8 ± 5.2

\*RRI, RR interval; HR, heart rate; SAP, systolic arterial pressure; DAP, diastolic arterial pressure; MAP, mean arterial pressure.

† $P < 0.05$  cervical vs thoracic.

‡ $P < 0.05$ ; || $P < 0.01$ ; ¶ $P < 0.001$  compared to resting values.

throughout the entire procedure, despite not having a history of previous cardiovascular disease (subject 1).

All arrhythmias noted in our study were self-terminating. No subject required cardiovascular intervention. No subject described symptoms associated specifically with the arrhythmia (although some subjects experienced facial flushing and upper body sweating associated with autonomic dysreflexia). At rest, 20% of individuals with thoracic SCI demonstrated arrhythmia, whereas none of the cervical subjects had arrhythmia at this time. During ejaculation, 50% of subjects with cervical, but none of the thoracic subjects, developed arrhythmia. During the recovery phase, 50% of cervical and 40% of thoracic subjects had arrhythmias. Figure 1 is an example of an ECG tracing during the vibrostimulation trial from a subject with C4 ASIA grade B SCI. This subject displayed normal sinus rhythm at rest, but during ejaculation and recovery, he exhibited frequent premature atrial contractions and junctional beats.

2. *Bradycardia.* Eleven individuals exhibited sinus bradycardia (usually related to high blood pressure associated with autonomic dysreflexia), often to very low heart rates, and in subject 2 to only 35 bpm. Bradycardia was an equally common finding among subjects with cervical and thoracic SCI throughout the vibrostimulation procedure. Bradycardia was particularly common during the recovery phase in those with thoracic SCI.

3. *Tachycardia.* Only one subject (subject 13) with thoracic SCI developed sudden-onset sinus tachycardia, to 120 bpm, during ejaculation.

## DISCUSSION

We have described for the first time the incidence of ECG abnormalities in individuals with SCI undergoing vibrostimulation. We found a high susceptibility to ECG

abnormalities during the procedure in SCI individuals, which may be related to level of SCI and/or to the presence or absence of SSR. In total, 11 out of the 13 SCI subjects studied had abnormal ECG findings induced at some stage during the procedure. The risk of developing ECG abnormalities was greatest during ejaculation and recovery. In addition, 10 out of the 13 subjects in this study developed autonomic dysreflexia during the procedure. Many of these men were unaware of the presence of arrhythmia or other ECG abnormalities and did not report symptoms associated with the episodes of autonomic dysreflexia, as has been noted recently (25,26). This study highlights the importance of an awareness of potential adverse cardiovascular events that may occur during vibrostimulation, which can be used to identify and prevent the development of these potentially life-threatening sequelae. In addition, since in many cases the subject experienced no symptoms associated with these adverse cardiovascular events, it may be advisable for men with SCI to be screened for potential cardiovascular events as part of their rehabilitation program to enable safe sexual practices, both at home and in the setting of a fertility clinic. Moreover, it may be that other stimuli below the level of the SCI (in addition to vibrostimulation, particularly if sufficient to induce autonomic dysreflexia) would also precipitate ECG abnormalities in individuals with SCI.

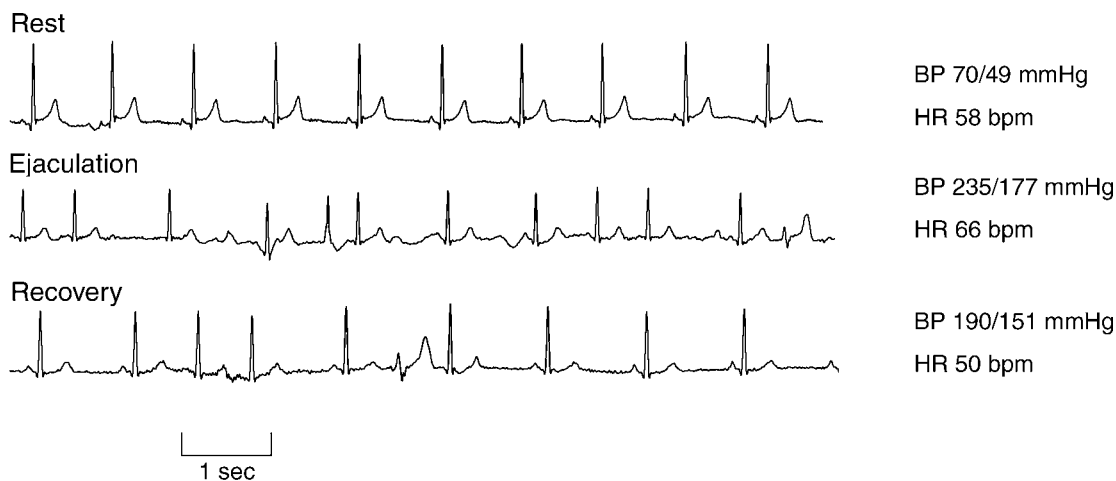
## Cardiovascular Control During Vibrostimulation

It is known from previous studies that at rest, individuals with SCI have a higher incidence of nonspecific ST elevation (and thus early repolarization) than do able-bodied individuals (6,7), and they are also reported to be at increased risk of developing ECG abnormalities, such as premature atrial contractions, intraventricular conduction delays, and bundle-branch blocks (2,3). Several studies have indicated that the incidence of arrhythmia in

**Table 4.** Arrhythmia and ECG Abnormalities Detected at Rest, During Vibrostimulation, Ejaculation, and Recovery\*

Subject	SCI	Rest	Vibrostimulation	Ejaculation	Recovery
1	C2 ASIA A	...	...	Sinus bradycardia	Sinus bradycardia with occasional junctional bradycardia
2	C4 ASIA A	Sinus bradycardia	Sinus bradycardia	Marked sinus bradycardia (35 bpm); frequent PAC	Sinus bradycardia; frequent PAC; occasional VE
3	C4 ASIA B	Sinus bradycardia	Sinus bradycardia	Sinus bradycardia	Sinus bradycardia
4	C4 ASIA B	Sinus bradycardia	...	Frequent PAC; multifocal VE; occasional nonconducted p waves	Occasional PAC; frequent VE
5	C4 ASIA B	Sinus bradycardia	Sinus bradycardia; occasional nonconducted p waves; VEx1; PACx1	Frequent PAC; frequent VE	Sinus bradycardia
6	C5 ASIA C	...	...	Sinus bradycardia	Sinus bradycardia
7	C6 ASIA A	...	VEx1	Sinus bradycardia; frequent PAC including bigeminy	Frequent PAC
8	C7 ASIA A	...	...	...	...
9	T3 ASIA A	...	...	...	Sinus bradycardia; frequent PAC
10	T4 ASIA A	Sinus bradycardia; VEx1; PACx1	...	Sinus bradycardia	Sinus bradycardia
11	T5 ASIA A	...	Sinus bradycardia; VEx1; frequent PAC	Sinus bradycardia	Sinus bradycardia
12	T6 ASIA A	Sinus bradycardia	Sinus bradycardia	Sinus bradycardia	Sinus bradycardia; couplet VE
13	T5 ASIA C	Sinus bradycardia	Sinus bradycardia; triplet PAC	Sinus tachycardia	...

\*VE, ventricular ectopic beats; PAC, premature atrial contractions.



**Figure 1.** Example ECG tracing from a 44-year-old man who sustained C4 ASIA B SCI following a motor vehicle accident. Both palmar and plantar SSR were absent. Heart rate (HR) and blood pressures (BP) during the different stages of the procedure can be seen to the right of the ECG tracings. This subject exhibited marked autonomic dysreflexia during ejaculation and developed frequent junctional beats and frequent premature atrial contractions.

patients with SCI (particularly bradyarrhythmias) is increased and that those with higher lesions are more at risk of developing bradyarrhythmias (9). It has also been suggested previously (8) that individuals with SCI are only at severe risk of developing arrhythmia during the acute phase of injury (and particularly during spinal shock). However, this is not necessarily the case, and there is at least one report of late asystole (5–9 weeks after the injury) sufficient to require transvenous ventricular pacing (27).

Furthermore, these studies have all examined the incidence of arrhythmia at rest, and few studies have investigated arrhythmia during cardiovascular stress or autonomic dysreflexia. However, there is some evidence to indicate, as reported in the present study, that autonomic dysreflexia may be associated with cardiac arrhythmias, particularly atrial fibrillation (4,5,28), which may require pharmacologic conversion to restore the normal rhythm (5). Furthermore, a case report in a young woman with SCI at the level of T5 describes profound cardiac irregularities during autonomic dysreflexia triggered by uterine contractions during labor, in which there was a clear relationship between the severity of autonomic dysreflexia and the arrhythmia (29). Certainly it is known that cardiovascular mortality is greater in individuals with SCI than in able-bodied persons (1,30), and these data indicate that the incidence of both ECG abnormalities and autonomic dysreflexia in individuals with chronic SCI may be underestimated.

The cardiovascular responses to vibrostimulation in this study were similar to those described in a previous report from our laboratory using predominantly the same subjects (20). Subjects with SCI in our study showed a marked rise in blood pressures and, often, signs of autonomic dysreflexia during vibrostimulation, which

persisted in many subjects during the recovery period, and this result is consistent with the findings of others (5,31,32). Also in line with these earlier studies, we often observed bradycardia associated with autonomic dysreflexia, although this was not always the case in the men with thoracic SCI. The development of autonomic dysreflexia was common in patients with both cervical and thoracic injuries, although it was more severe in subjects with higher level lesions or those involving destruction of the spinal autonomic pathways (as evidenced by the absence of SSR). This reinforces the need for investigators to monitor all subjects undergoing vibrostimulation for sperm retrieval for symptoms and signs of autonomic dysreflexia, with particular attention paid to those with high-level lesions or lesions involving the descending cardiovascular autonomic pathways.

The importance of understanding the abnormal cardiovascular regulation in individuals with SCI is dictated by clinical epidemiology data showing increased cardiovascular and cerebrovascular morbidity and mortality following SCI (1,33). The majority of risk factors are similar between able-bodied and SCI individuals. However, lack of exercise and unstable blood pressure control in SCI subjects could be additional contributing factors for their higher incidence of cardiovascular disorders. Furthermore, it has been suggested (34–36) that large swings in blood pressure (from resting hypotension to marked hypertension associated with autonomic dysreflexia) could result in increased shear stress and consequent endothelial damage, which would be likely to predispose these individuals to cerebrovascular events.

#### SSR and ASIA Scores

The SSR is an electrophysiological technique that records changes in skin conductance after activation of sweat

glands in plantar and palmar skin areas that are rich in eccrine glands (37). This response is thought to be under the neural control of sympathetic cholinergic (sudomotor) fibers (15,37). SCI results in disruption of the connections between the spinal sympathetic circuits and the corresponding supraspinal centers (the hypothalamus and brainstem), while the peripheral “end-organs” of the sympathetic system are not usually affected (12). Thus, in patients with complete high cervical injury, the SSR in the hands and feet following stimulation of any peripheral nerve are absent (15). For complete lesions between the levels of T4 and T7, the SSR in the feet are usually absent, while response in the hands may be preserved. In patients with complete lesions below the level of T7, the SSR in the hands and feet could be present. At present, the ASIA assessment is widely accepted as the standard neurological assessment of motor and sensory deficits occurring following SCI (14). However, this evaluation does not account for the degree of injury to spinal autonomic pathways (16). Thus, the autonomic pathways must be assessed by some other means, such as SSR testing. In this study we examined SSR and ASIA scores and confirmed early observations that the completeness of lesions as determined by ASIA score does not necessarily reflect the integrity of the descending autonomic pathways (38–40).

This study highlights the fact that the examination of neurological function following SCI should include not only motor and sensory assessment with ASIA score but also assessment of spinal autonomic pathways. Furthermore, we have confirmed previous reports in which abnormal SSR were associated with an increased risk of developing severe autonomic dysreflexia (18). One of the hypotheses of this study was that the destruction of spinal autonomic pathways (as assessed by SSR) would also be associated with an increased risk of developing arrhythmia during the vibrostimulation procedure. This was seen to be the case, particularly during ejaculation, during which individuals with SCI and absent SSR (and higher level injuries) were more prone to arrhythmias. It may be that individuals with SCI who are prone to episodes of autonomic dysreflexia (and thus those with injury to the descending spinal autonomic pathways) are more at risk of developing cardiac arrhythmias during these episodes.

### **Mechanisms of Arrhythmia in SCI**

The reasons for which men with SCI are at increased risk of developing ECG abnormalities during vibrostimulation are uncertain. We hypothesized that, at rest, those with absent palmar SSR (and, thus, presumably a loss of descending spinal sympathetic control of the heart) (15,40) would be at increased risk of developing arrhythmia through unopposed high vagal tone and associated bradyarrhythmias. In many (although not all) cases, the arrhythmias were associated with the presence of autonomic dysreflexia due to sympathetic hyperactivity, and it may be that

the extreme hypertension of autonomic dysreflexia activates a marked increase in vagal stimulation through the baroreflex (12), which in some individuals may predispose them to escape beats and ectopic beats (41–43). Furthermore, this unique state of combined sympathetic hyperactivity and high vagal tone associated with autonomic dysreflexia represents greatly disordered autonomic control of the heart and is likely to be proarrhythmogenic. It might seem from the data presented that this is an unlikely mechanism, since the heart rates reported were not usually that slow (and, hence, presumably the vagal tone was not that high). However, it should be noted that the heart rates stated are average values taken over 10 beats, and because of the presence of frequent atrial and ventricular ectopics, the heart rate data would reflect these additional beats. In addition, as mentioned previously, individuals with SCI have a higher incidence of ST elevation (and thus early repolarization) than do able-bodied individuals, which may also predispose individuals with SCI to arrhythmia (7).

### **Limitations**

There are a number of potential limitations to this study. There was no prior cardiovascular screening of the subjects. Ideally, 12-lead ECG examinations should have been performed on all subjects to examine whether there were any preexisting cardiovascular abnormalities that could predispose to arrhythmia *per se*. These data were not available for the present investigation. However, all subjects were questioned regarding their previous medical history, and none reported any known cardiovascular disease or defects.

It may be argued that the arrhythmias documented in the present study do not necessarily represent serious cardiovascular events, and thus that the implications of this work are small. It is true that none of the arrhythmias documented in this study represented serious cardiovascular events, and in no individual was it necessary to terminate the study as a result of cardiac arrhythmia (or autonomic dysreflexia). However, this does not necessarily mean that the implications of this work are limited. First, the presence of ventricular ectopic beats, particularly those occurring in couplets or triplets, and multifocal ventricular ectopics in otherwise healthy young men may represent a significant potential for that individual to develop more serious cardiovascular events (44). Likewise, frequent premature atrial contractions may predispose one to atrial fibrillation (45,46), which is known to be associated with serious cardiovascular and cerebrovascular events (47). Indeed, atrial fibrillation is documented in the SCI population during sperm retrieval (5) and autonomic dysreflexia (4,28). Second, the arrhythmias noted in the present study tended to occur concurrently with episodes of autonomic dysreflexia. Very few of the subjects in this study reported symptoms of autonomic dysreflexia during the procedure, and yet many were able to describe highly symptomatic episodes



of autonomic dysreflexia that occurred during daily life. If the incidence of arrhythmia were to be related to the severity of autonomic dysreflexia (and the extent and duration of the blood pressure rise), then it may be expected that the incidence of arrhythmia during these presumably more severe episodes of autonomic dysreflexia would be greater or more prolonged.

The other major concern with this study is the lack of a suitable control group. Unfortunately, again due in part to the retrospective nature of the data analyses, these data were not available. Furthermore, because of the sensitive nature of the study, the recruitment of healthy male volunteers to undergo these procedures is difficult. One study (31) indicates that the cardiovascular responses during and, in particular, after ejaculation in SCI subjects and able-bodied controls are quite different. However, they did not comment on whether there were ECG abnormalities or arrhythmias in either group during the procedure. A second study (48) examined the ECGs of 120 able-bodied control volunteers before and after (but not during) ejaculation and did not find any evidence of arrhythmia in these individuals. These data indicate that the responses seen in the SCI men in the present study are likely to be different in comparison to the responses of healthy, able-bodied men.

## CONCLUSION

SCI is associated with cardiovascular abnormalities, including arrhythmias that could potentially lead to more serious cardiovascular events. Vibrostimulation was associated with increased incidence of autonomic dysreflexia and arrhythmia in subjects with both cervical and thoracic SCI. The incidence of arrhythmia during ejaculation was greater in those with cervical than in those with thoracic injuries. Individuals with damage to descending spinal sympathetic pathways (as assessed from SSR) and/or high SCI may be prone to more severe autonomic dysreflexia and a greater incidence of arrhythmia. The mechanisms underlying the increased incidence of arrhythmia are uncertain, but they are likely to be related to the disordered sympathovagal balance that occurs during episodes of autonomic dysreflexia. We advocate that medical practitioners performing vibrostimulation (and other procedures likely to induce autonomic dysreflexia) in individuals with SCI should be aware of the potential for these individuals to develop cardiac arrhythmias. Appropriate cardiovascular monitoring, if available, may provide a prudent safety precaution during such procedures.

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