Cardiovascular Physiology and Responses to Sexual Activity in Individuals Living with Spinal Cord Injury

Ross Davidson, MD,^{1,2} and Aaron Phillips, PhD^{1,2}

¹International Collaboration On Repair Discoveries, Vancouver, BC, Canada; ²Faculty of Medicine, Division of Physical Medicine and Rehabilitation, University of British Columbia, British Columbia, Canada

Background: Spinal cord injury (SCI) may profoundly impact autonomic function producing a variable degree of dysfunction in cardiovascular, bronchopulmonary, sweating, bladder, bowel, and sexual function. The cardiovascular system is crucially important for sexual function, as it is responsible for blood flow shifts to cavernous and musculoskeletal tissue during sexual activity. This system is prone to 3 main abnormalities after SCI including low resting blood pressure (LRBP), orthostatic hypotension (OH), and autonomic dysreflexia (AD), all of which have important effects on sexual function. **Methods:** We review the current etiological mechanisms and manifestations of cardiovascular dysfunction after SCI and discuss how this is documented to impact sexual function in individuals living with SCI. **Conclusions:** All individuals with SCI at or above the T6 neurologic level have an increased risk of AD during sexual stimulation, with increasing risk associated with higher levels of injury and greater completeness of injury. AD can be silent, and individuals living with SCI should be aware of blood pressure values at baseline and during sexual activity. Clinicians performing vibrostimulation fertility procedures need to be aware of the risk of AD and consider pretreatment if needed. Researchers studying the cardiovascular response to sexual stimulation should consider continuous monitoring of blood pressure, as intermittent monitoring may underestimate true blood pressure values. **Key words:** autonomic function, cardiovascular disease, fertility interventions, sexual health, spinal cord injury

Spinal cord injury (SCI) is a worldwide public health concern and is a cause of permanent disability in younger and older individuals.¹ Advances in emergent therapies, early hospitalization, surgical care, rehabilitation, and management of secondary conditions have led to higher survival rates and a greater life expectancy in people who have sustained an SCI.² With improved survival rates, the importance of living well with SCI and maximizing quality of life has become of paramount importance.

The spinal cord contains ascending and descending tracts of nerve fibers along with clusters of motor, sensory, and autonomic nuclei. After injury, any and all of these structures can be damaged to various degrees and affect motor, sensory, and autonomic function.³ Motor and sensory dysfunction is most often discussed as a target for recovery, and it is perhaps the most visible element of SCI; however impairment secondary to loss of autonomic function can be profound and greatly impact an individual's ability to live well with SCI.

Autonomic function is a broad term that encompasses several different body functions coordinated by the autonomic nervous system. This includes the control of heart rate (HR), blood pressure (BP), sweating, pulmonary secretory and bronchodilatory function, control of bladder and bowel function, and sexual function.^{3,4} The autonomic nervous system has 2 divisions including parasympathetic and sympathetic systems, which generally oppose each other to create a balance depending on the stimulus provided. Important exceptions include peripheral blood vessels and adrenal glands, which generally are only influenced by the sympathetic nervous system.⁵

The sympathetic nervous system communicates with end organs in 2 ways, locally via thoracolumbar projections from the spinal cord releasing norepinephrine from postganglionic sympathetic neurons, and via the blood stream through the soluble neurotransmitter epinephrine and to a lesser extent norepinephrine. In contrast, the parasympathetic nervous system communicates

Corresponding author: Ross Davidson, MD, International Collaboration On Repair Discoveries, 818 West 10th Avenue, Vancouver, BC, V5Z 1M9 Canada; phone: 778-987-2771; e-mail: ross.davidson@vch.ca

Top Spinal Cord Inj Rehabil 2017;23(1):11–19
© 2017 Thomas Land Publishers, Inc.
www.thomasland.com

doi: 10.1310/sci2301-11

with end organs via craniosacral projections from the brain and spinal cord, including the vagus nerve, which innervates intraabdominal and intrathoracic organs down to the level of the splenic flexure of the large intestine or colon, including the ascending and transverse sections. The descending colon is innervated by parasympathetic projections from the sacral spinal cord.^{4,5}

For individuals living with SCI, sexual function has been identified as a priority for recovery. Sexuality is a universal and integral part of the human experience and persists in individuals well beyond reproductive years in both good and failing health.^{6,7} When surveyed about the priority of various body functions to restoration of quality of life, men and women with SCI reported that the restoration of sexual function was either the first or second highest priority (second only to restoration of hand function in those living with quadriplegia); it was prioritized even above the return of walking, sensation, and normal bowel and bladder function.⁷ As clinicians and scientists, we must assist individuals living with SCI in restoring these functions in a way that improves quality of life and prevents further health issues.

Cardiovascular autonomic function has an important role in facilitating sexual activity. It is integral in coordinating blood flow shifts during sexual activity to cavernous tissue and active skeletal muscle in response to genital arousal and movement associated with sexual activity. In individuals living with SCI, autonomic physiology is altered to varying degrees; as a result, low resting blood pressure (LRBP), orthostatic hypotension (OH), and autonomic dysreflexia (AD) may be barriers to or consequences of sexual activity that must be contended with and compensated for in order to enhance this function and quality of life.^{8,9}

AD is of particular interest during sexual activity, as this phenomenon may be triggered by the intense sensory input associated with sexual stimulation. The consequent increase in BP may be a hazard to the individual. This review will explore the interaction between the aberrations in cardiovascular physiology that are known to occur following SCI and sexual activity and will provide clinicians working with individuals living with SCI recommendations for ways to compensate for and avoid issues related to LRBP, OH, and AD during

sexual activity and during reproductive procedures such as penile vibratory stimulation (PVS) and electroejaculation (EEP).

Cardiovascular Consequences Following SCI

Over the past 10 years, what we know about the underlying pathophysiology of AD after SCI has been greatly enhanced.¹⁰⁻¹³ The most prominent outcomes of mechanistic maladaptations described above are LRBP¹⁴ and extremely labile BP characterized by frequent and pronounced episodes of low BP when an individual assumes an upright position (OH) and episodes of dangerously high BP in response to afferent stimuli below the level of injury (AD). These cardiovascular conditions will be discussed in detail throughout the next sections.

Low resting blood pressure

In addition to hypotension experienced during the acute period following SCI (neurogenic shock), individuals with high thoracic and cervical SCI frequently have BP at rest that is significantly lower than in able-bodied individuals.¹⁵ Clinical evidence indicates that the extent and severity of hypotension correlates well with the level and severity of SCI.^{12,16-18} In the non-SCI population, an “inverted-U relationship” exists between resting BP and overall health, which means that in addition to the well-established risks associated with high BP, there are also significant clinical conditions associated with too low BP.¹⁹⁻²¹

Low BP has now been shown to be associated with clinical conditions in the SCI population, in whom impaired cerebrovascular and cognitive function are associated with LRBP.²² LRBP after SCI is also associated with a number of other conditions, including exacerbated dizziness, development of syncope, poor mood, lethargy, and fatigue.²³⁻²⁷ Considering this, the risk of low BP should be appreciated, and LRBP should be clinically addressed in persons with SCI.

AD

Episodes of AD are characterized by an acute elevation of systolic BP (SBP) of at least 20 mm Hg,

which may or may not be accompanied by a decrease in HR.²⁸ Episodes of AD occur in response to afferent stimuli that would be considered painful or nonpainful visceral or somatic stimulation below injury, including a full bladder, bowel, or sexual activity (**Figure 1**). Episodes of AD can occur in both the acute and chronic phases of SCI.^{29,30} In fact, SBP can rise above 300 mm Hg during AD.³¹ In the chronic phase of SCI, episodes of AD occur up to 41 times per day (average of 11 times per day) in the majority of persons with high-level SCI above the T5 level.³² Episodes of AD are often, but not always, accompanied by a pounding headache and flushing above the injury.^{14,28,33} Left untreated, episodes of AD could result in life-threatening complications, including cerebral hemorrhage, retinal detachment, seizures, cardiac arrhythmias, and death.^{31,34,35}

The most common stimuli to trigger AD is bladder and bowel distention, but AD can also be brought on by sexual stimulation, spasms, pressure sores, and even something as simple as a tight shoe lace.³⁶ AD can also result from catheterization and/or the manipulation of an indwelling catheter, urinary tract infection, detrusor sphincter dyssynergia, and bladder percussion. There are also a number of iatrogenic triggers including cystoscopy, PVS or EEP, and the electrical stimulation of muscles.³⁷⁻³⁹ The intensity of AD episodes is variable, with not all episodes being severe, especially if the triggering stimulus is promptly resolved. In fact, many AD episodes are asymptomatic (ie, the patient does not recognize AD even though BP is increasing) or are characterized by sweating and/or piloerection alone.⁴⁰ The level and completeness of

the injury are the primary determinants for the presence and severity of AD. For example, AD is 3 times more common in individuals with complete versus incomplete quadriplegia⁴¹ and typically occurs when the SCI is at or above the T6 spinal segments.^{36,42} As will be discussed below, changes in the autonomic circuits in the spinal cord are major contributing factors to the development of AD.¹¹

OH

Episodes of OH are characterized by drastic reductions in BP when an individual assumes the upright posture. The interruption of sympatho-excitatory pathways after SCI (from the brainstem to the end organs) impairs the capacity of the arterial baroreflex to efficiently cause vasoconstriction and maintain BP.^{43,44} Although the cardiovagal baroreflex is impaired after SCI, the sympathetic system is primarily responsible for BP maintenance during an orthostatic challenge. It needs to be appreciated that it is only during the first 2 to 3 seconds after an orthostatic challenge that the cardiovagal effect on HR impacts BP stability.⁴⁵⁻⁴⁸ The result is low venous return secondary to blood pooling in the vasculature caudal to the site of injury and low arterial BP/vessel tone.⁴⁸ Additionally, there are low resting catecholamine levels after cervical SCI and no discernable increase with supraspinal sympathetic activation induced by upright tilt.⁹ Stiffer central arteries (that are responsible for detecting BP changes) after SCI further impairs baroreflex function.⁴⁹ OH is most common and severe in the acute phase of SCI, but it also can be observed in the chronic phase among

Figure 1. Autonomic dysreflexia during sexual stimulation. Blood pressure (BP) tracing during penile vibrostimulation in a male with a motor complete C5 SCI. Within 60 seconds, systolic BP rises to above 225 mm Hg. Transient elevations in BP of this nature may lead to cardiovascular or cerebrovascular events, whereas repetitive exposure to these events may create a predisposition to increasing risk of cardiovascular diseases.

individuals with high cervical SCI.^{23,50} Similar to resting BP, the severity and level of injury to descending sympatho-excitatory pathways is directly associated with OH,²⁴ indicating again that the extent of cardiovascular instability after SCI is related to the completeness of injury to autonomic pathways within the spinal cord.

OH is defined as a decrease in SBP of at least 20 mm Hg or a decrease in DBP of at least 10 mm Hg when assuming an upright posture from the supine position, regardless of presence of symptoms.⁵¹ The Consensus Committee of the American Autonomic Society and the American Academy of Neurology agreed upon this definition.⁵¹ Presyncopal symptoms in persons living with SCI are similar to those experienced in the able-bodied population⁵² and include light-headedness, dizziness, blurred vision, fatigue, nausea, dyspnea, and restlessness.^{53,54} On top of this, OH was demonstrated to be a causal factor in cognitive decline after SCI.²⁷

OH is extremely common in people living with SCI, with up to 74% of individuals during the acute period of SCI experiencing OH when they perform orthostatic maneuvers during physical therapy and mobilization.²⁵ OH does not always lead to presyncopal symptoms, and more than 40% of persons with SCI are asymptomatic during episodes of OH.⁹ OH often persists into the chronic stage of SCI, however presyncopal symptoms may subside partially.⁹ In the chronic SCI phase, OH occurs in up to 50% of cervical SCI patients and 18% of thoracic SCI patients; however, from this "OH-positive" group, presyncopal symptoms were only present in one-third and one-fifth of individuals, respectively.⁹ Reduced symptoms of presyncope, but similar OH, in the chronic phase of SCI suggest that tolerance to low BP and cerebral perfusion pressure may improve with time after injury.^{26,55,56} Considering the association between OH and an elevated risk of stroke in the non-SCI population,⁵⁷ as well as the fact that stroke risk is 3 to 4 times greater after SCI, it is logical to posit that the presence of OH after SCI plays a contributing role in stroke.^{58,59}

Other factors contributing to the presence of OH after SCI include reduced plasma volumes due to hyponatremia,⁵³ insufficient increases in renin-angiotensin system to maintain BP,⁶⁰ and potentially

cardiac deconditioning.⁶¹⁻⁶³ Similar effects from these mechanisms also lead to LRBP after SCI.¹⁴

To summarize, episodes of OH can lead to cognitive decline, syncope, nausea, fatigue, and dizziness while significantly impeding rehabilitation, including sexual function. Over the long-term, OH likely contributes to an elevated risk of stroke after SCI. Resting hypotension may also play a role in cognitive dysfunction by exacerbating the severity of OH and the ensuing cerebral hypoperfusion. The detailed mechanisms related to LRBP, AD, and OH have recently been reviewed by Phillips and Krassioukov.⁶⁴

Cardiovascular Responses to Sexual Activity

Various models of sexual function describe the stages that humans progress through during sexual arousal.^{65,66} The classic model published by Masters and Johnson describes excitement, plateau, orgasm, and resolution phases based on laboratory observations of physiologic parameters they observed in over 600 healthy subjects of varying ages. Masters and Johnson noted that men generally progress through the 4 phases more quickly than women, often with a very short plateau phase, and achieve only one orgasm per cycle due to a refractory period after orgasm. In contrast, women were observed to have the potential to achieve multiple orgasms per cycle without a refractory period. Both sexes had the potential to fluctuate between excitement and plateau without carrying on to orgasm.

Data from Masters and Johnson indicated a rise in both HR and BP in men and women during the excitement and plateau phases, peaking at or slightly after orgasm. Of all the phases, the orgasmic phase was the shortest, lasting only 10 to 15 seconds for men and 20 to 60 seconds for women.⁶⁵ During this time, HR and BP were noted to be at their peak. Throughout subsequent years of study, various laboratory and home-based methods of measuring cardiovascular parameters during sexual activity in physiologically normal individuals found modest increases in HR, SBP, and DBP, approximately equal to between 2 and 4 METs of metabolic demand.⁶⁷⁻⁷¹

Cardiovascular responses to sexual activity follow a less predictable and more labile pattern

in people living with SCI than in able-bodied individuals. Individuals living with lesions at or above the T6 spinal level are predisposed to episodes of AD,⁶⁴ and sexual stimulation can be a potent trigger of this phenomenon.⁷² The next section of this review will discuss changes in cardiovascular parameters during specific sexual stimuli in individuals with SCI.

Cardiovascular responses during self-stimulation

The cardiovascular responses to self-stimulation in males and females living with SCI have been investigated.^{71,73-75} In one study performed by Sipski et al,⁷¹ 45 men with a variety of SCI levels and completeness of injury were investigated using intermittent BP monitoring every 3 minutes during a self-stimulation protocol. There were no significant changes in either BP or HR values as subjects progressed from the excitement, plateau, and orgasm phases as measured with a visual scale of subjective arousal. None of the subjects described symptoms of AD in this study. Using a similar protocol with intermittent BP recordings, Sipski et al⁷⁴ studied the cardiovascular responses to manual self-stimulation in 13 women with incomplete SCI above the T6 level. This group found nonsignificant, modest increases in SBP and HR, with no one reporting typical AD symptoms during the study. Given previous findings that peak BP tends to dissipate within 1 to 2 minutes, and due to intermittent BP measurements only being taken every 3 minutes, it is possible that maximum peak BPs may have been missed during both of these studies and consequently not reported.

Cardiovascular changes during intercourse

Few studies exist that directly measure BP and HR changes in response to sexual intercourse in individuals with SCI. A case report by McBride et al⁷² measured an episode of severe AD and arrhythmia with a maximum SBP of 325 mm Hg in a man with long-standing tetraplegia in response to stimulation by his partner. Another report describes AD in one subject that had its onset in response to sexual activity with a partner at home.⁷⁶

These reports, and numerous anecdotal patient testimonials, confirm that AD as the result of sexual activity occurs in individuals with SCI. Bolstering this evidence, a survey of women living with SCI conducted by Charlifue et al found that AD is an unwanted consequence of sexual activity in up to 27% of females living with SCI.⁸ A report by Anderson et al describes that AD during sexual activity is interpreted negatively by many individuals with SCI and can interfere with sexual activity.^{7,77} These reports however do not quantify the exact changes in BP or HR.

Cardiovascular responses during PVS procedures

PVS is a fertility procedure that involves placing a specially designed vibrating device on the glans penis with the ability to change the frequency and amplitude of the stimulus delivered to accomplish ejaculation.³³ The duration of application of the generally ranges between 3- and 5-minute intervals, with multiple attempts if needed. This intense stimulus is strong enough to cause skin irritation and breakdown and is a potent trigger for AD. Studies of PVS in individuals at risk for AD that monitor BP continuously reveal peak SBP of 65 to 107 mm Hg above baseline, occurring at or near ejaculation.^{33,39,76,78,79} This is in contrast to studies that measure BP intermittently, which only report peak SBP of 40 to 50 mm Hg above baseline during procedures.⁸⁰⁻⁸³ The latter estimate may be considered less accurate because SBP changes on a beat-to-beat basis³³ and intermittent monitoring can miss the peak BP depending on whether the reading was observed just before, during, or after ejaculation.

Likewise, the studies also describe a wide variety of HR responses, ranging from a reduction of 17.5 bpm in HR below baseline during AD⁸⁴ to an increase of 13 bpm above baseline.⁷⁸ As noted earlier, individuals with an injury at or above T6 are more likely to experience more severe episodes of AD; this finding is consistent with the literature investigating the cardiovascular response to sexual activity in individuals living with SCI.^{33,78,81}

The variability in reported peak SBP in the literature has given rise to disagreement regarding how severe the SBP increases during PVS can be. Some studies⁸¹⁻⁸³ report an average peak SBP

of 156 mm Hg in individuals with cervical SCI. In contrast, other studies^{76,78,79} that record BP continuously report a noticeably higher average peak SBP during PVS ranging from an increase of 10 mm Hg up to 107 mm Hg above baseline. The only major difference between these experimental studies was the method of BP monitoring. Because of the variability in BP increases and the associated AD, first time use of PVS for men should be done under clinical conditions to monitor the severity of the BP rise, regardless of symptoms.⁴⁰

Limited data exist for the incidence of AD during vibrostimulation sperm retrieval trials in which vibrostimulation may be less intense and at home where commercially available vibrostimulatory devices are used.⁸⁵ It is likely that the intensity of AD in individuals with SCI who use commercially available vibrators would be less compared to that of PVS, as the intensity of the stimulus is less. However, it is not known just how much less.

Cardiovascular responses during EEP

EEP requires the use of a rectal probe to deliver current to the periprostatic nerves in order to induce an ejaculatory specimen. The procedure is utilized for fertility purposes in men with SCI. An early report of AD during EEP was published in 1974; Frankel et al described uncontrolled hypertension brought on during an EEP.⁸⁶ It has since been well accepted that this stimulus can be a potent trigger of AD and associated arrhythmia, requiring cardiac monitoring and pretreatment with antihypertensive medication.⁸⁷ For this reason, EEP is usually performed in a clinical setting or operating room where cardiovascular parameters can be closely monitored and medical assistance with BP can be applied as necessary.

Clinical Recommendations

Autonomic cardiovascular control may be significantly altered after SCI and become a barrier to sexual function in addition to the impairments in sexual function that are associated with SCI. Numerous cardiovascular maladaptations after SCI contribute to the development of LRBP, OH, and AD. AD may be triggered by sexual stimulation and appears to be more common in individuals with

higher levels and completeness of injury. AD also may be more common with increased intensity of stimulus such as during PVS or EEP. From this evidence, a few clinical recommendations can be made.

All people with SCI who have a neurologic level of injury at or above T6 are at risk for AD. The risk increases with higher levels of injury and greater completeness of the injury. AD has characteristic symptoms that individuals living with SCI should be aware of; however, AD can be silent, and all individuals at risk of AD should be aware of their own resting BP and BP during sexual activity to prevent the associated complications of AD.

Certain types of sexual stimulation such as PVS or EEP are extremely intense, and BP monitoring is mandatory during these procedures to guide the clinician and prevent injury. If BP rises acutely to unsafe levels, the procedure should be stopped. The acute BP value considered “dangerous” in an able-bodied population of 200/110 mm Hg may not be valid in people living with SCI; these individuals may have LRBP and therefore the BP usually considered normal for able-bodied individuals may be very elevated for individuals with a resting BP below 90 mm Hg.

Continuous BP monitoring during procedures such as PVS and EEP are superior to intermittent, noninvasive monitoring. This is because the intermittent nature of measurements may miss peaks and valleys in BP and may make it difficult for the clinician to make an accurate assessment about when additional trials of PVS or EEP are safe or unsafe. Further research regarding PVS should use continuous monitoring to avoid confusion in the literature regarding the true rise in BP during these procedures.

For individuals with known symptomatic AD, or silent AD that brings BP values into an unsafe range, pretreatment with medication is indicated. A variety of options are available, and evidence exists for prazosin and nifedipine.^{87,88} Prazosin is preferred as it poses a lower risk of creating symptomatic drops in BP.

Conclusions

SCI can result in profound alterations in cardiovascular autonomic function resulting in LRBP, OH, and AD. The mechanisms underlying

these abnormalities are myriad and include sympathetic preganglionic plasticity, dorsal root afferent and intraspinal neuron plasticity below the level of injury, and peripheral vascular hyperresponsiveness.⁶⁴ Aberrant cardiovascular physiology may interfere with sexual function in individuals living with SCI by producing AD during self-stimulation, intercourse, and during fertility procedures. The cardiovascular responses are most studied during the latter 2 procedures; further study is needed to characterize the exact changes in

cardiovascular parameters during self-stimulation and intercourse in this population. Medical professionals who are involved with PVS or EEP procedures must pay attention to cardiovascular parameters, preferably by using continuous BP monitoring during the procedure, and they should stop the procedures if unsafe BPs arise. Pretreatment with prazosin or nifedipine is indicated for persons who are known to have severe AD in the interest of avoiding complications and maintaining long-term cardiovascular health of these individuals.

REFERENCES

- Noonan VK, Fingas M, Farry A, et al. Incidence and prevalence of spinal cord injury in Canada: A national perspective. *Neuroepidemiology*. 2012;38(4):219-226.
- Consortium for Spinal Cord Medicine. Outcomes following traumatic spinal cord injury: Clinical practice guidelines for health-care professionals. *J Spinal Cord Med*. 2000;23(4):289-316.
- Meston CM, Frohlich PF. The neurobiology of sexual function. *Arch Gen Psychiatry*. 2000;57(11):1012.
- Krassioukov A. Autonomic function following cervical spinal cord injury. *Respir Physiol Neurobiol*. 2009;169(2):157-164.
- Krassioukov A, Biering-Sorensen CF, Donovan W, et al. International Standards to document remaining Autonomic Function after Spinal Cord Injury (ISAFSCI), First Edition 2012. *Top Spinal Cord Inj Rehabil*. 2012;18(3):282-296.
- Field-Fote, E. *Spinal Cord Injury Rehabilitation*. Philadelphia: FA Davis; 2009.
- Anderson KD, Borisoff JF, Johnson RD, Stiens SA, Elliott SL. The impact of spinal cord injury on sexual function: Concerns of the general population. *Spinal Cord*. 2007;45(5):328-337.
- Charlifue SW, Gerhart KA, Menter RR, Whiteneck GG, Manley MS. Sexual issues of women with spinal cord injuries. *Paraplegia*. 1992;30(3):192-199.
- Claydon VE, Krassioukov AV. Orthostatic hypotension and autonomic pathways after spinal cord injury. *J Neurotrauma*. 2006;23(12):1713-1725.
- de Groat WC, Yoshimura N. Mechanisms underlying the recovery of lower urinary tract function following spinal cord injury. *Prog Brain Res*. 2006;152:59-84.
- Krassioukov AV, Johns DG, Schramm LP. Sensitivity of sympathetically correlated spinal interneurons, renal sympathetic nerve activity, and arterial pressure to somatic and visceral stimuli after chronic spinal injury. *J Neurotrauma*. 2002;19(12):1521-1529.
- Mathias CJ, Bannister SR. *Autonomic Failure: A Textbook of Clinical Disorders of the Autonomic Nervous System*. Oxford: Oxford University Press; 2013.
- Teasell RW, Arnold JM, Krassioukov A, Delaney GA. Cardiovascular consequences of loss of supraspinal control of the sympathetic nervous system after spinal cord injury. *Arch Phys Med Rehabil*. 2000;81(4):506-516.
- Krassioukov A, Claydon VE. The clinical problems in cardiovascular control following spinal cord injury: An overview. *Prog Brain Res*. 2006;152:223-229.
- West CR, Mills P, Krassioukov AV. Influence of the neurological level of spinal cord injury on cardiovascular outcomes in humans: A meta-analysis. *Spinal Cord*. 2012;50(7):484-492.
- Hadley MN. Blood pressure management after acute spinal cord injury. *Neurosurgery*. 2002;50(3):S58-S62.
- Nacimiento W, Noth J. What, if anything, is spinal shock? *Arch Neurol*. 1999;56(8):1033-1035.
- Vale FL, Burns J, Jackson AB, Hadley MN. Combined medical and surgical treatment after acute spinal cord injury: Results of a prospective pilot study to assess the merits of aggressive medical resuscitation and blood pressure management. *J Neurosurg*. 1997;87(2):239-246.
- Duschek S, Schandry R. Cognitive performance and cerebral blood flow in essential hypotension. *Psychophysiology*. 2004;41(6):905-913.
- Duschek S, Hadjamu M, Schandry R. Enhancement of cerebral blood flow and cognitive performance following pharmacological blood pressure elevation in chronic hypotension. *Psychophysiology*. 2007;44(1):145-153.
- Hebert LE, Scherr PA, Bennett DA, et al. Blood pressure and late-life cognitive function change: A biracial longitudinal population study. *Neurology*. 2004;62(11):2021-2024.
- Phillips AA, Warburton DER, Ainslie PN, Krassioukov AV. Regional neurovascular coupling and cognitive performance in those with low blood pressure secondary to high-level spinal cord injury: Improved by alpha-1 agonist midodrine hydrochloride. *J Cereb Blood Flow Metabol*. 2014;34(5):794-801.
- Cariga P, Ahmed S, Mathias CJ, Gardner BP. The prevalence and association of neck (coat-hanger) pain and orthostatic (postural) hypotension in human spinal cord injury. *Spinal Cord*. 2002;40(2):77-82.
- Claydon VE, Steeves JD, Krassioukov A. Orthostatic hypotension following spinal cord injury:

- Understanding clinical pathophysiology. *Spinal Cord*. 2006;44(6):341-351.
25. Illman A, Stiller K, Williams M. The prevalence of orthostatic hypotension during physiotherapy treatment in patients with an acute spinal cord injury. *Spinal Cord*. 2000;38(12):741-747.
 26. Phillips AA, Krassioukov AV, Ainslie PN, Warburton DER. Perturbed and spontaneous regional cerebral blood flow responses to changes in blood pressure after high-level spinal cord injury: The effect of midodrine. *J Appl Physiol*. 2014;116(6):645-653.
 27. Wecht JM, Bauman WA. Decentralized cardiovascular autonomic control and cognitive deficits in persons with spinal cord injury. *J Spinal Cord Med*. 2013;36(2):74-81.
 28. Krassioukov A, Warburton DE, Teasell R, Eng JJ. A systematic review of the management of autonomic dysreflexia after spinal cord injury. *Arch Phys Med Rehabil*. 2009;90(4):682-695.
 29. Ekland MB, Krassioukov AV, McBride K, Elliott SL. Incidence of AD and Silent AD in men with SCI undergoing sperm retrieval: Implications for clinical practice. *J Spinal Cord Inj Med*. 2008;31:33-39.
 30. Krassioukov A. Autonomic dysreflexia in acute spinal cord injury: Incidence, mechanisms, and management. *SCI Nurs*. 2004;21(4):215-216.
 31. Wan D, Krassioukov AV. Life-threatening outcomes associated with autonomic dysreflexia: A clinical review. *J Spinal Cord Med*. 2014;37(1):2-10.
 32. Hubli M, Gee CM, Krassioukov AV. Refined assessment of blood pressure instability after spinal cord injury. *Am J Hypertens*. 2015;28(2):173-181.
 33. Claydon VE, Elliott S, Sheel W. Cardiovascular responses to vibrostimulation for sperm retrieval in men with SCI. *J Spinal Cord Inj Med*. 2006;1-10.
 34. Pine ZM, Miller SD, Alonso JA. Atrial fibrillation associated with autonomic dysreflexia. *Am J Phys Med Rehabil*. 1991;70(5):271-273.
 35. Zhang Y, Guan Z, Reader B, et al. Autonomic dysreflexia causes chronic immune suppression after spinal cord injury. *J Neurosci*. 2013;33(32):12970-12981.
 36. Teasell RW, Arnold JMO, Krassioukov A, Delaney GA. Cardiovascular consequences of loss of supraspinal control of the sympathetic nervous system after spinal cord injury. *Arch Phys Med Rehabil*. 2000;81(4):506-516.
 37. Chang CP, Chen MT, Chang LS. Autonomic hyperreflexia in spinal cord injury patient during percutaneous nephrolithotomy for renal stone: A case report. *J Urol*. 1991;146(6):1601-1602.
 38. Giannantonio A, Di Stasi SM, Scivoletto G, et al. Autonomic dysreflexia during urodynamics. *Spinal Cord*. 1998;36:756-760.
 39. Sheel AW, Krassioukov AV, Inglis JT, Elliott SL. Autonomic dysreflexia during sperm retrieval in spinal cord injury: Influence of lesion level and sildenafil citrate. *J Appl Physiol*. 2005;99(1):53-58.
 40. Kirshblum SC, House JG, O'Connor KC. Silent autonomic dysreflexia during a routine bowel program in persons with traumatic spinal cord injury: A preliminary study. *Arch Phys Med Rehabil*. 2002;83(12):1774-1776.
 41. Curt A, Nitsche B, Rodic B, Schurch B, Dietz V. Assessment of autonomic dysreflexia in patients with spinal cord injury. *J Neurol Neurosurg Psych*. 1997;62(5):473-477.
 42. Mathias CJ, Frankel HL, Christensen NJ, Spalding JM. Enhanced pressor response to noradrenaline in patients with cervical spinal cord transection. *Brain*. 1976;99(4):757-770.
 43. Blackmer J. Rehabilitation medicine: 1. Autonomic dysreflexia. *CMAJ*. 2003;169(9):931-935.
 44. Claydon VE, Hol AT, Eng JJ, Krassioukov AV. Cardiovascular responses and postexercise hypotension after arm cycling exercise in subjects with spinal cord injury. *Arch Phys Med Rehabil*. 2006;87(8):1106-1114.
 45. Ogoh S, Fadel PJ, Nissen P, et al. Baroreflex-mediated changes in cardiac output and vascular conductance in response to alterations in carotid sinus pressure during exercise in humans. *J Physiol*. 2003;550(Pt 1):317-324.
 46. Ogoh S, Volianitis S, Nissen P, Wray DW, Secher NH, Raven PB. Carotid baroreflex responsiveness to head-up tilt-induced central hypovolaemia: Effect of aerobic fitness. *J Physiol*. 2003;551(Pt 2):601-608.
 47. Ogoh S, Yoshiga CC, Secher NH, Raven PB. Carotid-cardiac baroreflex function does not influence blood pressure regulation during head-up tilt in humans. *J Physiol Sci*. 2006;56(3):227-233.
 48. Phillips AA, Krassioukov AV, Ainslie PN, Warburton DER. Baroreflex function after spinal cord injury. *J Neurotrauma*. 2012;29(15):2431-2445.
 49. Phillips AA, Cote AT, Bredin SSD, Krassioukov AV, Warburton DER. Aortic stiffness increased in spinal cord injury when matched for physical activity. *Med Sci Sports Exerc*. 2012;44(11):2065-2070.
 50. Mathias CJ. Orthostatic hypotension: Causes, mechanisms, and influencing factors. *Neurology*. 1995;45(suppl 5):S6-S11.
 51. Kaufmann H. Consensus statement on the definition of orthostatic hypotension, pure autonomic failure and multiple system atrophy. *Clin Auton Res*. 1996;6(2):125-126.
 52. Cleophas TJ, Kauw FH, Bijl C, Meijers J, Stapper G. Effects of beta adrenergic receptor agonists and antagonists in diabetics with symptoms of postural hypotension: A double-blind, placebo-controlled study. *Angiology*. 1986;37(11):855-862.
 53. Frisbie JH, Steele DJ. Postural hypotension and abnormalities of salt and water metabolism in myelopathy patients. *Spinal Cord*. 1997;35(5):303-307.
 54. Sclater A, Alagiakrishnan K. Orthostatic hypotension. A primary care primer for assessment and treatment. *Geriatrics*. 2004;59(8):22-27.
 55. Horowitz DR, Kaufmann H. Autoregulatory cerebral vasodilation occurs during orthostatic hypotension in patients with primary autonomic failure. *Clin Auton Res*. 2001;11(6):363-367.
 56. Phillips AA, Ainslie PN, Krassioukov AV, Warburton DER. Regulation of cerebral blood flow after spinal cord injury. *J Neurotrauma*. 2013;30(18):1551-1563.
 57. Eigenbrodt ML, Rose KM, Couper DJ, Arnett DK, Smith R, Jones D. Orthostatic hypotension as a risk factor

- for stroke: The atherosclerosis risk in communities (ARIC) study. *Stroke*. 2000;31(10):2307-2313.
58. Cragg JJ, Noonan VK, Krassioukov A, Borisoff J. Cardiovascular disease and spinal cord injury: Results from a national population health survey. *Neurology*. 2013;81(8):723-728.
 59. Wu J-C, Chen Y-C, Liu L, et al. Increased risk of stroke after spinal cord injury: A nationwide 4-year follow-up cohort study. *Neurology*. 2012;78(14):1051-1057.
 60. Groothuis JT, Thijssen DHJ, Rongen GA, et al. Angiotensin II contributes to the increased baseline leg vascular resistance in spinal cord-injured individuals. *J Hypertens*. 2010;28(10):2094-2101.
 61. Shibata S, Perhonen M, Levine BD. Supine cycling plus volume loading prevent cardiovascular deconditioning during bed rest. *J Appl Physiol* (1985). 2010;108(5):1177-1186.
 62. Vaziri ND. Nitric oxide in microgravity-induced orthostatic intolerance: Relevance to spinal cord injury. *J Spinal Cord Med*. 2003;26(1):5-11.
 63. West CR, Crawford MA, Laher I, Ramer MS, Krassioukov AV. Passive hind-limb cycling reduces the severity of autonomic dysreflexia after experimental spinal cord injury. *Neurorehabil Neural Repair*. 2016;30(4):317-327.
 64. Phillips AA, Krassioukov AV. Contemporary cardiovascular concerns after spinal cord injury: Mechanisms, maladaptations, and management. *J Neurotrauma*. 2015;32(24):1927-1942.
 65. Masters WH, Johnson VE. *Human Sexual Response*. Boston: Little, Brown; 1966.
 66. Basson R. Women's sexual dysfunction: Revised and expanded definitions. *CMAJ*. 2005;172(10):1327-1333.
 67. Bohlen JG, Held JP, Sanderson MO, Patterson RP. Heart rate, rate-pressure product, and oxygen uptake during four sexual activities. *Arch Int Med*. 2008;144:1745-1748.
 68. Chen X, Zhang Q, Tan X. Cardiovascular effects of sexual activity. *Ind J Med Res*. 2010;1-8.
 69. Kruger T, Exton M, Pawlak C, zur Muhlen von A, Hartmann U, Schedlowski M. Neuroendocrine and cardiovascular response to sexual arousal and orgasm in men. *Psychoneuroendocrinology*. 1998;23(4):401-411.
 70. Exton MS, Bindert A, Kruger T, Scheller F, Hartmann U, Schedlowski M. Cardiovascular and endocrine alterations after masturbation induced orgasm in women. *Psychosomatic Med*. 1999;61:280-289.
 71. Sipski M, Alexander CJ, Gómez-Marín O. Effects of level and degree of spinal cord injury on male orgasm. *Spinal Cord* 2006;44(12):798-804.
 72. McBride F, Quah SP, Scott ME, Dinsmore WW. Tripling of blood pressure by sexual stimulation in a man with SCI. *J Royal Soc Med*. 2003;96(7):349-350.
 73. Sipski M, Alexander CJ, Rosen RC. Orgasm in women with spinal cord injury, a laboratory based assessment. *Arch Phys Med Rehabil*. 1995;76(12):1097-1102.
 74. Sipski M, Alexander C, Rosen R. Physiological parameters associated with psychogenic sexual arousal in women with complete SCI. *Arch Phys Med Rehabil*. 1995;76(9):811-818.
 75. Whipple B, Gerdes C, Komisaruk B. Sexual response to self-stimulation in women with complete SCI. *J Sex Res*. 1996;33(3):231-240.
 76. Elliott SL, Krassioukov A. Malignant autonomic dysreflexia in spinal cord injured men. *Spinal Cord*. 2006;44(6):386-392.
 77. Anderson KD, Borisoff JF, Johnson RD, Stiens SA, Elliott SL. Spinal cord injury influences psychogenic as well as physical components of female sexual ability. *Spinal Cord*. 2007;45(5):349-359.
 78. Brown R, Stolzenhein G, Engel S, Macefield VG. Cutaneous vasoconstriction as a measure of incipient autonomic dysreflexia during penile vibratory stimulation in spinal cord injury. *Spinal Cord*. 2008;47(7):538-544.
 79. Ekland MB, Krassioukov A, McBride K, Elliott S. Incidence of AD and silent AD in men with SCI undergoing sperm retrieval: Implications for clinical practice. *J Spinal Cord Inj Med*. 2008;31(1):33-39.
 80. Soler JM, Previnaire JG, Plante P, Denys P, Chartier-Kastler E. Midodrine improves ejaculation in spinal cord injured men. *J Urol*. 2007;178(5):2082-2086.
 81. Courtois FJ, Charvier KF, Leriche A, Vézina J-G, Côté M, Bélanger M. Blood pressure changes during sexual stimulation, ejaculation and midodrine treatment in men with spinal cord injury. *BJU Int*. 2008;101(3):331-337.
 82. Courtois F, Charvier K, Leriche A, et al. Perceived physiological and orgasmic sensations at ejaculation in spinal cord injured men. *J Sex Med*. 2008;5(10):2419-2430.
 83. van Middendorp JJ, Hosman AJ, Donders AR, et al. A clinical prediction rule for ambulation outcomes after traumatic spinal cord injury: A longitudinal cohort study. *Lancet*. 2011;377(9770):1004-1010.
 84. Courtois F, Geoffrion R, Landry É, Bélanger M. A clinical prediction rule for ambulation outcomes after traumatic spinal cord injury: A longitudinal cohort study. *Lancet*. 2011;377(9770):1004-1010.
 85. Naphtali K, MacHattie E, Elliott S, Krassioukov A. *PleasureABLE, Sexual Device Manual for Persons with Disabilities*. 1st ed. Vancouver: Disabilities Research Health Network; 2009:1-25.
 86. Frankel HL, Mathias CJ, Walsh JJ. Blood pressure, plasma catecholamines and prostaglandins during artificial erection in a male tetraplegic. *Paraplegia*. 1974;12(3):205-211.
 87. Steinberger R, McCabe M, Ohl D, Bennet C. Nifedipine pre-treatment for AD during PVS in SCI. *Urology*. 1990;36(3):1-4.
 88. Zheng MM, Phillips AA, Elliott SL, Krassioukov AV. Prazosin: A potential new management tool for iatrogenic autonomic dysreflexia in individuals with spinal cord injury? *Neural Regen Res*. 2015;10(4):557-558.