Case-Based Learning Module: AUTONOMIC DYSREFLEXIA

INTRODUCTION

Autonomic Dysreflexia (AD) may present in patients with spinal cord injury at or above T6 (has been reported as low as T10).[1] AD must be treated immediately. This module will focus on the pathophysiology, causes and treatment of AD in a primary care setting. Example cases highlight common presentation, investigations and treatment of AD.
This module will enable clinicians to:

- Understand it as a serious medical condition
- Identify individuals who may be at risk and the presentation(s) of AD
- Understand triggers for AD, prevention and management
- Understand when to refer to specialists

CASE

Aaron, age 36

Aaron is a 36 year old paraplegic patient of your family medicine practice. He has an injury at the T1 level sustained 6 months ago in a motor vehicle accident. He has an appointment with you in the office to discuss recurrent headaches he is having. He reports he experienced occasional headaches before the accident, but these are different and worrisome to him as they come on very quickly and can be quite intense. He mentions that he has gone to the emergency department and his university healthcare clinic on two separate occasions and was given pain medications that seemed to help after some time.

What additional information from Aaron should you ask for?

- *He indicates that it is a pounding headache throughout his head, redness of his face, he feels very anxious when it comes on.*
- *It initially started as mild and maybe monthly but it is becoming more frequent to the point of almost daily. He is not sure of everything that might trigger it but has noticed a trend when his bladder has been very full. He has found emptying his bladder seems to help relieve his symptoms.*
- *You ask him about his bladder routine and he indicates he does clean intermittent catheterization about two to three times per day. He has started back at university a few months ago and he is finding it difficult to find places or time to empty bladder as frequently.*

What physical examination would be indicated?

- *You perform a neurological examination including cranial nerves which appears normal apart from his neurological deficits relating to his paraplegia. His cardiovascular and respiratory examination are normal. His blood pressure is 100/70, heart rate 80 and regular and respiratory rate 16.*

What is your differential diagnosis?

- *Migraine*
- *Cluster Headache*
- *UTI*

INFORMATION SECTION

Introduction

AD is a syndrome of imbalanced reflex sympathetic discharge occurring in patients with spinal cord injury (SCI) above the splanchnic sympathetic outflow (at or above the level of T6, but has been reported as low as T10).[1] AD may also be called autonomic hyperreflexia, and lifetime frequency has ranged from 19-70% in some studies[2,3] to 50-90% in individuals with tetraplegia or high paraplegia.[4]

Pathophysiology:

AD results from an unbalanced physiologic response to a noxious or non-noxious stimulus below the level of spinal cord lesion (see Figure 1). The stimulus results in a peripheral sympathetic response through spinal reflexes, causing vasoconstriction below the level of injury. The reflex response travels both up and down the spinal cord through paraspinal sympathetic ganglia, resulting in both direct vasoconstriction via activation of perivascular receptors and systemic/indirect vasoconstriction through stimulation of the adrenal medulla, causing epinephrine and norepinephrine release into the systemic circulation. These signals result in hypertension, primarily through splanchnic and peripheral vasoconstriction.[5] Barorecptors in the carotid and aortic arch sense the increase in BP and activate parasympathetic nerves above the level of the lesion to counter the sympathetic response.[6] The CNS is unable to directly detect the strong or noxious signal below the level of injury because of the lack of continuity of the ascending sensory fibers from the spinal cord injury, and, therefore, respond to hypertension by sending an inhibitory response through the spinal cord in order to decrease the resulting sympathetic response [5] (see Table 1 for signs and symptoms of AD).

Differential Diagnoses:[8]

- Migraine
- Cluster headache
- Essential hypertension
- Posterior fossa tumour
- Phaeochromocytoma
- Toxemia of pregnancy

Clinical Pearl: AD should be treated immediately; identifying and removing the stimulus can alleviate signs and symptoms.

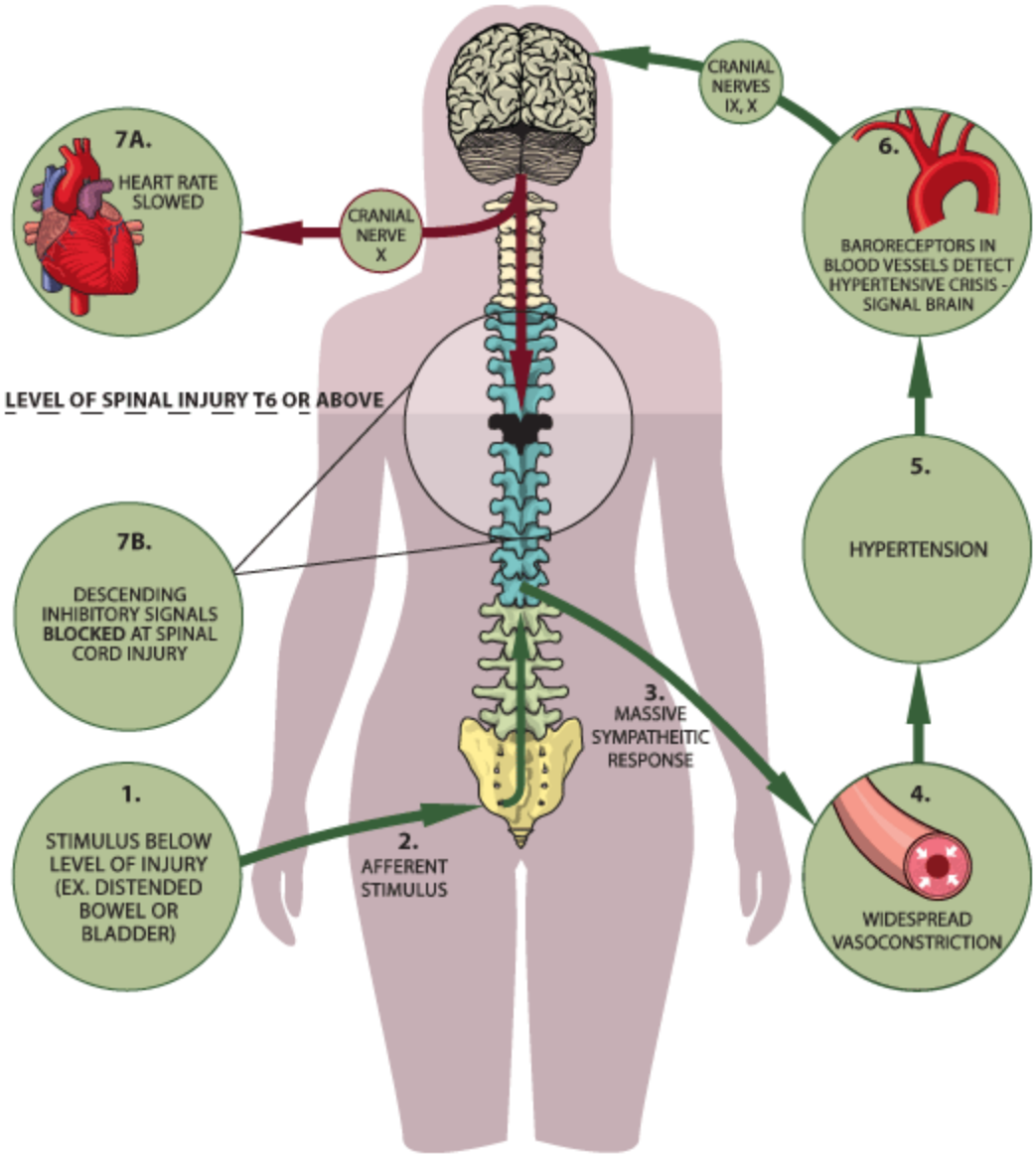

Figure 1: Diagram illustrating the mechanism of autonomic dysreflexia in a person with spinal cord injury. The afferent stimulus (a distended bladder, above) triggers a peripheral sympathetic response resulting in vasoconstriction and hypertension. The descending inhibitory signals, which would normally counteract the rise in blood pressure, are unable to pass the level of the spinal cord injury. The roman numerals (IX, X) refer to the glossopharyngeal and vagus nerves, respectively.[9]

Possible Outcomes of AD:

Individuals with higher level lesions of the spinal cord are normally hypotensive with normal blood pressures ranging between 90-110/60 mmHg. AD can result in a rise of >20 mmHg above what is normal for the individual. If AD is not relieved and blood pressure rises, it can lead to intracranial haemorrhage, encephalopathy, myocardial infarction, seizures, and death.

Table 1: Signs and Symptoms of Autonomic Dysreflexia [5,12-14]

May involve all or some of the following:
BP elevated by 20-40 mmHg above patient's baseline*
Pounding headache
Bradycardia relative to patient's resting heart rate
Flushing of the face
Profuse sweating above the level of the lesion
Skin pallor, cold & piloerection (goosebumps) below the level of the lesion
Blurred vision
Shortness of breath
Anxiety
Nasocongestion
Cardiac arrhythmias, atrial fibrillation, premature ventricular contractions & atrioventricular conduction abnormalities

*Normal BP for an individual with a high level SCI will be 90-110/60 mmHg; therefore, a reading of 120-130/80 may be a sign of an episode of AD

Causes of AD:

It is caused by noxious or non-noxious stimuli below the level of the lesion. The most common causes are bladder or bowel irritation (see Table 2 for Causes of AD). Since AD can be relieved by finding and removing the stimulus, it is important to understand and check for these. Start by examining the urinary system/catheter and if acute AD symptoms persist, suspect fecal impaction.[10] Episodes of AD can vary in severity of signs and symptoms as well as length; although most cases are short lived due to treatment or self-limiting nature, there have been cases that can last hours to days. If BP is not elevated, but signs and symptoms of AD are present & the cause has not been identified, refer the patient to the appropriate consultant depending on symptoms.[10]

Table 2: Common Causes of Autonomic Dysreflexia[5,12]

Bladder	Distended or hyperactive bladder Urinary Tract Infection Catheterization Catheter tube kinking Bladder or Kidney stones
Bowel/Gastrointestinal	Constipation Faecal impaction Rectosigmoid gaseous distension Hemorrhoids Fissures Manual disimpaction Appendicitis Cholecystitis Esophageal reflux
Skin	Pressure areas Ingrown toenail Tight clothing/stockings/straps Blisters Burns
Other	Fracture Heterotopic ossification Hip dislocation Epididymoorchitis Sexual stimulation/intercourse Sexually Transmitted Infection (STI) Scrotal compression (sitting on scrotum) Labour or severe menstrual cramping • Women with spinal cord injury above the level of T6 who are pregnant may experience AD as the first sign as the commencement of labour • During labour and delivery, the risk of AD in patients with lesions at or above T6 is 85%-90% Deep vein thrombosis/Pulmonary embolism

Monitor vitals or patient for at least 2 hours after AD

AD can often be resolved if the noxious stimuli can be relieved

Non-Pharmacological Intervention[13]

Initial intervention should involve sitting the patient in the upright position, and physically examining the individual with SCI for the potential cause for the episode of AD. If BP has not begun to drop, loosen any tight clothing and/or constrictive devices. If these measures fail and the patient's BP continues to be at or above 150 mmHg in adults, 120 mmHg in children under 5 years old, 130 mmHg in children 6-12 years old, and 140 mmHg in adolescents, pharmacological agents should be initiated.[10]

Pharmacological Intervention:

There is no consensus on the timing of the use of medications for AD, but Clinical Practice Guidelines[10] suggest that if the BP remains elevated at or above 150 mmHg systolic, consider pharmacological measures in order to avoid the effects of hypertension while continuing to search for the cause. Antihypertensives with quick onset and short duration should be used. There is little research into the optimal antihypertensive, but common choices include:

- Nitroglycerin 0.4 mg/spray sublingually (1 spray q 5-10 min x3)
  OR
  Nitroglycerin ointment (1-2" ribbon applied above the level of the lesion, can be wiped off if becomes hypotensive)
    - **ensure no PDE5 inhibitor use in past 24** (for sildenafil or vardenafil) - **48h** (for tadalafil)
- Captopril 25 mg tablet
    - Take sublingually (dissolves in 3 minutes under tongue; spit out remainder if rapid hypotension occurs)
    - Effective in 15 minutes
- Nifedipine 10 mg capsule
    - "bite and swallow" (regular, not extended release)
    - Some reports of stroke, MI, death and severe hypotension in non-SCI studies has prompted caution with its use

Nitroglycerin spray might also be a consideration for many office based practices as it might be something that is already considered for stocking in an emergency kit.[11]

MONITOR FOR HYPOTENSION IF PHARMACOTHERAPY USED

- If hypotension experienced, have patient lie flat and raise the patient's leg

IF NOXIOUS STIMULUS CANNOT BE RELIEVED OR BP NOT CONTROLLED THEN PATIENT SHOULD GO TO EMERGENCY ROOM

Clinical Pearl: Nitroglycerin can usually be found in office treatment kits for acute MI. Be sure to regularly check expiry dates of medication prior to administration.

Figure 2: Acute Management of Autonomic Dysreflexia[12]

Encounter patient with BP > 20 mmHg above normal and signs and symptoms are suggestive of AD

↓

Inquire about AD susceptibility and what they think the trigger might be (ask about history of AD, wallet card, medic alert bracelet)
Call for assistance (**do not leave the patient alone)**

↓

Sit patent upright and lower legs (promotes blood pooling in the legs)
Remove restrictive clothing, socks, shoes and straps

↓

Monitor BP and HR **every 2-5 minutes**

↓

Check and remove noxious stimuli:

- Bladder (**most common cause**) – catheter kink, possible UTI, bladder distension
- Bowel – constipation, hemorrhoids, fecal impaction
- Skin – pressure ulcer, irritation, ingrown toenail
- Other causes (see common causes of AD)

↓ →

If patient is unstable (failure of BP to decrease, confusion, chest pain, decreased responsiveness) - **IMMEDIATELY CALL 911**

If systolic BP remains > 150 mmHg or there are persistent Symptoms, consider pharmacotherapy if needed (look in Emergency kit):

Nitroglycerin 0.4 mg/spray (will put shelf life here)
1 spray every 5 minutes up to 3 times as needed

or

~1-2 inches 2% nitroglycerin paste/ointment (applied above the level of spinal cord lesion)

Ensure no PDE5 inhibitor use in past 24h (sildenafil or vardenafil) – 48h (tadalafil) if using any nitroglycerin treatment

or

Captopril, 25 mg sublingually

or

Nifedipine, 10 mg "bite and swallow"

↙ ↘

BP and HR normal, noxious stimulus and symptoms resolved

- Monitor vital signs for 2-48h

AD persists or noxious stimulus not found

↓

- Post-care education & preventive strategies Send patient to Emergency Department

There has been some controversy about nifedipine possibly causing hypotension, cerebrovascular accident, myocardial infarction, and death when used in hypertensive emergencies; caution with nifedipine use might therefore be necessary

Following an Episode of Autonomic Dysreflexia:

After removing the noxious stimulus and AD has been resolved, monitor the patient for at least 2 hours to ensure that it does not reoccur (as it may be the medication that has caused BP to decrease and treatment may begin to reverse within this time frame).[10] If there is a poor response to treatment, if there cause of AD has not been identified or if there is suspicion of an obstetrical complication, consider referring the patient to hospital for monitoring[10]. It is important to document the episode of AD, including; how the patient presented (signs and symptoms), BP and pulse, treatment given, response to treatment and if a cause was determined. If a cause has been determined, once the patient is stabilized, review the cause with the patient, their family members, spouse and/or caregiver(s).[10] Prior to discharge, it is important to discuss prevention of AD in the future. If an individual experiences an episode of AD that resolves without presenting to a primary care provider's office, they must follow up with a medical professional, even if the episode resolves without requiring treatment.

Prevention of Autonomic Dysreflexia:

1. Education of patient and providers
2. Supplies at home: BP cuff, catheter supplies, short acting hypertensive
3. Warnings in patient chart
4. AD wallet card or MedicAlert bracelet

AD can be prevented by controlling noxious stimuli below the level of the lesion. Prevention measures include, but are not limited to; regularly scheduled bladder and bowel voiding, pressure techniques, and referral to chiropody for avoidance of ingrown toenails. Adjustment of the patient's treatment plan may be necessary to avoid future episodes of AD.[10] Education may also be required to help the patient minimize risks and recognize symptoms in the future. See Common Causes of Autonomic Dysreflexia for other areas of prevention.

Clinical Pearl: Ensure patients susceptible to AD are educated about the signs and symptoms and encourage carrying an AD wallet card and/or wearing a MedicAlert bracelet.

When to Refer:

- Frequent episodes of AD
- Severe episodes of AD
- Unknown triggers of AD
- Management of secondary conditions that trigger AD

CASE CONTINUED

Part 2

Aaron returns in follow up a week later, he is late by 10 minutes coming from university. He reports that he has generally felt better. He has been emptying his bladder more frequently and this seems to have helped. However, he reports he does have a moderate pounding headache right now, his vision is blurry, and he is feeling anxious. You notice that his face is flushed and there is sweat on his forehead.

What do you think is happening?

- *Autonomic dysreflexia*

What would you do now?

- *You take his blood pressure and heart rate which are 150/100 and 60 respectively. He is fully oriented, neurological and cardiorespiratory examination are normal. He feels uncomfortable when you palpate his lower abdomen. His extremities are normal except his legs feel cold. You ask Aaron when he last emptied his bladder and he reports it has been over 6 hours.*

You ask Aaron to catheterize himself, he does this and within minutes his symptoms start to lessen. You monitor his vital signs which return to his baseline within five minutes.

What are future plans for Aaron?

- *You have his vitals monitored for another thirty minutes in the office and since stable, then ask him to monitor when he goes home for at least 2 hours.*
- *You explain autonomic dysreflexia to him and give him resources including where to print out a wallet card to present to healthcare providers if needed.*
- *You review his bladder management and importance of frequent intermittent catheterization, plus other potential triggers. You book a follow up appointment in 2 weeks to review his progress.*

SUMMARY

- AD may present in individuals with SCI at T6 or above (has been reported as low as T10)
- Individuals with high level SCI will normally have a BP of 90-110/60 mmHg
- Increases of BP >20 mmHg may be indicative of an episode of AD
- Table 1 for Signs and Symptoms of AD
- Urinary system/catheter is most common cause of AD
- Table 2 for other Common Causes of AD
- See Acute Management of AD algorithm
- If source of AD not found and the patient is not responding to pharmacological intervention, immediately call 911
- Any episode of AD needs to be followed up by a medical professional
- See When to Refer

AD Wallet Card from: http://www.pva.org/spinal-cord/common-injury-complications

Common Warning Signs

DYSREFLEXIA

- A fast, major increase in blood pressure—20-40 mm Hg systolic higher than usual.
- A pounding headache
- Heavy sweating
- Flushed or reddened skin
- Goose bumps

- Blurry vision or seeing spots
- A stuffy nose
- Anxiety or jitters
- Tightness in your chest, flutters in your heart or chest, or trouble breathing

To obtain a complete guide, call toll-free (888) 860-7244 or www.pva.org

. Sit up or raise your head to 90 degrees. **Important:** You need to stay sitting or upright until your blood pressure is normal.
. Loosen or take off anything tight.
. Monitor your blood pressure about every 5 minutes.
. Check your bladder for drainage.
. Call your health-care professional, even if warning signs go away.
. If warning signs return, repeat steps, call your health-care professional, and go to the emergency room.
. At the emergency room, tell staff you need immediate care:
  - May have dysreflexia.
  - Need blood pressure checked.
  - Need to remain sitting up.
  - Need causes of the problem sought.

REFERENCES

1. Moeller Jr. BA, & Scheinber D. (1973). Autonomic Dysreflexia in injuries below the sixth thoracic segment (letter). Journal of the American Medical Association 224(9):1295.
2. Braddom RL, & Rocco JF. (1991). Autonomic dysreflexia. A survey of current treatment. *American Journal of Physical Medicine & Rehabilitation* 70: 234-241.
3. Snow JC, Sideropoulos HP, Kripke BJ, Freed MM, Shah NK, & Schlesinger FM. (1978). Autonomic hyperreflexia during cystoscopy in patients with high spinal cord injuries. *Paraplegia* 15: 327-332.
4. Vaidyanathan S. (2012). Autonomic dysreflexia in a tetraplegic patient due to a blocked urethral catheter: spinal cord injury patients with lesions above T-6 require prompt treatment of an obstructed urinary catheter to prevent life-threatening complications of autonomic dysreflexia. *Journal of Emergency* Medicine 5(6): 1-5.
5. Stephenson RO, & Klein MJ. (2016). Autonomic Dysreflexia in Spinal Cord Injury. Medscape. Obtained from http://emedicine.medscape.com/article/322809-overview#a1 on December 14, 2016.
6. .Milligan J, Lee J, McMillan C, & Klassen H. (2012). Autonomic dysreflexia. *Canadian Family Physician* 58(8): 831-835.
7. Brown R, Burton A, Macefield VG. (2009). Input-output relationships of a somatosympathetic reflex in human spinal injury. *Clinical Autonomic Research* 19(4): 213-220
8. Lee BY, Karmakar MG, Herz BL, & Sturgill RA. (1994). Autonomic dysreflexia revisited. *Journal of Spinal Cord Medicine* 18: 75-87.
9. Blackmer, J. (2003). Rehabilitation medicine: 1. Autonomic dysreflexia. Canadian Medical Association Journal 169(9): 931-935.
10. Consortium for Spinal Cord Medicine. Acute management of autonomic dysreflexia: individuals with spinal cord injury presenting to health-care facilities. (2002). *Journal of Spinal Cord Medicine* 25(1): 67-88.
11. A Practical Guide for Safe and Effective Office-Based Practices. College of Physicians and Surgeons of Ontario. May 2012; Preparing for a medical emergency- Anticipating the unexpected in an office or clinic. CMPA. January 2013.
12. Milligan J, Lee J, McMillan C, & Klassen H. (2012). Recognizing a common serious condition in spinal cord injured patient. Canadian Family Physician 58(8): 831-835.
13. Paralyzed Veterans of America. Clinical practice guidelines. http://www.pva.org/site/c.ajIRK9NJLcJ2E/b.6305831/k.986B/Guidelines_and_Publications.htm
14. SCIRE (Spinal Cord Injury Rehabilitation Evidence) http://scireproject.com/rehabilitation-evidence

FURTHER READING

1. Bauman C, Milligan J, Lee J, & Riva JJ. (2012). Autonomic dysreflexia in spinal cord injury patients: an overview. The Journal of the Canadian Chiropractic Association 56(4): 247-250.
2. Consortium for Spinal Cord Medicine: Clinical Practice Guidelines. (2001). Acute Management of Autonomic Dysreflexia: Individuals with Spinal Cord Injury Presenting to Health-Care Facilities. Spinal Cord Medicine.
3. Krassioukov A, Warburton DE, & Eng JJ. (2009). A systematic review of the management of autonomic dysreflexia after spinal cord injury. Archives of Physical Medicine and Rehabilitation 90: 682-695.
4. Middleton J, Ramakrishnan K, & Cameron I. (2013). Treatment of Autonomic Dysreflexia for Adults & Adolescents with Spinal Cord Injuries. NSW Agency for Clinical Innovation.
5. Rabchevsky AG, & Kitzman PH. (2011). Latest approaches for the treatment of spasticity and autonomic dysreflexia in chronic spinal cord injury. Neurotherapeutics 8: 274-282.