

Narcolepsy: Information for Physicians



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Summary: Narcolepsy is a sleep condition with excessive, sometimes (or often) disabling sleepiness, no matter how much sleep one gets. Classic symptoms include sleep attacks, cataplexy (muscle weakness with strong emotions), hypnagogic/hypnapompic hallucinations and sleep paralysis. Treatment includes lifestyle modifications; medications such as stimulants, modafinil and others.

Case

Jennifer is in her 20's and has extreme problems with sleepiness. This is extremely frustrating, because when younger, she was extremely active and athletic. Nowadays however, no matter how much sleep she gets at night, she is always exhausted. The sleepiness is so bad that she'll fall asleep on public transit, and even while talking with friends. It is so bad that she couldn't finish high school, and hasn't been able to keep any job due to her fatigue and inability to wake up on time for work. Due to the impairment in work and relationships, she is feeling anxious and depressed. She has seen counselors for depression and feels guilty that she was not able to follow their advice with behavioural activation. She has seen doctors and been tested for hormone, vitamin deficiencies and diet issues, but no one has found anything. Her diagnosis so far is "treatment-resistant depression."

What is Narcolepsy?

Narcolepsy is a sleep disorder that consists of a classic pentad:

1. Excessive daytime sleepiness

- It can range from mild "mental cloudiness" to irresistible sleepiness that makes it impossible to function.
- Unrefreshing sleep: Even when they appear to get what seems to be enough hours of sleep, it is not refreshing. And despite feeling sleepy throughout the day, people have poor night-time sleep, with repeated awakenings, sometimes with vivid dreams. "A whole night's sleep can feel like a five minute nap -- and a five-minute nap can feel like a whole night's sleep."
- Uncontrollable "sleep attacks": Sleep attacks are irresistible urges to sleep, and one simply falls asleep during any activity, at any time during the day. Understandably, this can cause severe problems with school, work and home life.

2. Cataplexy:

- Sudden brief episodes of muscle weakness that occur with a strong emotional trigger.
- Triggers include laughter, surprise, anger, extreme happiness or sadness. Examples of muscle weakness include knees buckling, or the head drooping, or even speech becoming slurred because of an inability to move muscles necessary for speech. Some people experience full-body episodes where they are unable to move or verbally communicate.
- Duration: Attacks last from a few seconds to several minutes.
- Differential diagnosis of cataplexy
 - People may fall to the ground because of the knees buckling, misleading some observers to believe that the person has fainted or had a seizure -- in cataplexy, consciousness is maintained throughout the spell.
- Etiology of cataplexy
 - Thought to be related to the muscle paralysis of REM sleep intruding abnormally in wakefulness.
- Up to 70% of those with narcolepsy have cataplexy, which can manifest together with daytime sleepiness, or develop later, even 5-10 years after sleepiness occurs. Cataplexy is very specific to narcolepsy -- it is rarely seen in those without narcolepsy.

3. Hypnopompic or Hypnagogic Hallucinations

- Vivid and frightening hallucinations, e.g. seeing bugs on the walls, or hearing noises in the home. People often worry that they are going "crazy" and are worried to mention these symptoms.
- Hallucinations may happen upon going to sleep (hypnagogic), or upon awakening from sleep (hypnopompic).
- These are also thought to be examples of REM sleep phenomena (in this case dream content) intruding upon wakefulness.
- Up to 60% of those with narcolepsy have these experiences, often frightening.
- People without narcolepsy sometimes have sleep paralysis and/or hypnagogic / hypnopompic hallucinations especially if they are extremely sleep deprived. These people, however, will not have cataplexy.

4. Sleep paralysis

- Periods where one feels suddenly unable to move, or speak, or sometimes even breathe for seconds or minutes, though it often feels much longer, occurring upon awakening or just before falling asleep.
- Sleep paralysis can be quite terrifying.
- The paralysis is thought to be the muscle paralysis normally confined to REM sleep intruding upon wakefulness.
- Most people with narcolepsy (i.e. 60%) will experience this symptom, but this can also occur in those without narcolepsy.

5. Difficulty maintaining sleep

- Although patients with narcolepsy have significant sleepiness during the day, they can have very fragmented sleep at night.
- This is thought to represent not only sleepiness intruding upon wakefulness (i.e. feeling sleepy during the day), but also wakefulness intruding upon sleep (i.e. inability to maintain sleep during the night).

As a result, narcolepsy can cause significant problems with all aspects of life including school, work, relationships and home life.

Epidemiology

Prevalence

- 1 in 2000 people (0.05% of the population).

Onset

- Symptoms can start at any age, but most often starts in adolescence.
- Peak periods of onset appear to be age 15 and age 35 (Dauvilliers, 2001).

Etiology

Narcolepsy is believed to be caused by:

- Autoimmune disorder. It may start with a viral infection, or other stress on the body's immune system, but in other cases the cause is unknown. In certain cases, the body's immune system ends up attacking the brain cells that produce hypocretin (aka orexin), which is a neurotransmitter that helps regulate the state between sleep and wake. As a result, when the brain lacks hypocretin, there is significant difficulty regulating sleep and wakefulness -- so e.g. REM sleep intrudes into normal waking periods and vice versa.
- Genetics: Narcolepsy may also be genetic in the case of 1-2% of family members who have this condition.

Assessment / History

Red Flags and Screening Questions

Symptom	Screening Question
Excessive sleepiness:	Do you feel excessive sleepiness all the time, even when you have gotten an appropriate amount of sleep in the night?
Cataplexy	When you have a strong emotion (e.g. like telling a joke, or someone telling you something funny, or when you get surprised, angry or sad), do your muscles get weak? (e.g. like your neck might droop, you might have trouble speaking, you might drop something, or you fall down?)
Hypnagogic (hallucinations while going to sleep) or /hypnopompic hallucinations (hallucinations while waking up from sleep)	Ever see or hear things while falling asleep or waking up? (e.g. bugs on the walls, hearing sounds)
Sleep paralysis	Ever feel paralyzed when waking or falling asleep?

Screening Tools

Sleep Disorders Symptom Checklist-25 (SDS-25)

Consider the SDS-25, which is a 25-item screener developed for primary care providers, which allows differentiation of insomnia, circadian rhythm, narcolepsy, obstructive sleep apnea, restless legs syndrome, and parasomnias.

<https://www.sleepmedres.org/journal/view.php?number=90>

Differential diagnoses (DDx)

Rule out persistent sleepiness and fatigue due to other causes such as:

Sleep issues

Chronic Insufficient sleep,	What is the bedtime? What is the wakeup time?
Obstructive sleep apnea	Is there snoring?
Inadequate sleep hygiene	Is there an inconsistent sleep schedule? E.g. Staying up to watch screens? Napping during the day?
Circadian rhythm sleep wake disorder, delayed sleep phase type	Are there difficulties initiating sleep, accompanied by , difficulties waking up in the morning?
Periodic limb movement disorder	Are there periodic episodes of repetitive limb movements while asleep? Have others noted jerky movements while asleep? Kicking at night? Are sheets and blankets all over the place, or all messed up in the mornings?

Sleepiness due to use of mood altering medications	Is there excess use of medications that might affect sleep? (e.g. tobacco, caffeine, alcohol, stimulants, cannabis, opioids etc.)
Restless legs syndrome (RLS), aka Willis Ekbohm Disease	Are there uncomfortable sensations in the legs, especially when sitting or lying? Are these sensations relieved with movement? Is the urge to move worse at night?
Idiopathic hypersomnia	Excessively sleeping during the day? Troubles being woken up? Have all other causes been ruled out? If so, consider idiopathic hypersomnia.

Mental health conditions

Depression	Troubles with depressed mood? Problems with sleep, concentration, appetite, energy, loss of interests? Thoughts of suicide or self harm? Difficulty sleeping at night?
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Medical conditions.

Anemia	Does exercise lead to unusually rapid heart rate, shortness of breath, headache? Pale skin? Low iron diet? Fatigue? Low energy?
Thyroid issues	Fatigue? Sensitivity to cold? Constipation? Dry skin? Weight gain? Muscle weakness?
Diabetes	Increased thirst? Frequent urination? Extreme hunger? Unexplained weight loss? Fatigue? Irritability?

Investigations

Consider:

- Iron levels
- Thyroid levels
- Glucose

Is narcolepsy suspected?

- If so, then refer to a sleep clinic for assessment and consideration for a multiple sleep latency test (MSLT)
 - MSLT is performed after an overnight sleep study (PSG or polysomnogram).
 - The MSLT is a daytime sleep test, where people are given 4-5 opportunities to have a nap (lasting up to 35 minutes), each separated by 2 hour intervals.
 - Depending on how quickly the patient falls asleep and whether or not the patient reaches REM sleep, it can be determined if the patient has narcolepsy.
 - The combination of a mean sleep latency of less than eight minutes plus at least two naps with a sleep onset REM period is consistent with narcolepsy (American Academy of Sleep Medicine, 2005).

Management: Non-Medication

Behavioural approaches

- Ensure good quality sleep at night.
- Nap of 15-20 minute in the afternoon.

Address any other sleep disorders (such as sleep apnea).

Management: Self-Help and Lifestyle Strategies

With narcolepsy, most likely medications will be required. Nonetheless, lifestyle interventions are important, because even with treatment, many people with narcolepsy may still struggle with symptoms.

- Keep a regular sleep-wake schedule; avoid jobs that require irregular sleep schedules (i.e. shift work).
- Don't stay up late, even on weekends.

- Avoid alcohol and other central nervous system depressants.
- Take intentional short naps (10-30 minutes) as needed to avoid unintentional sleep attacks.
- Use modest amounts of caffeine to promote alertness as needed.
- Need to drive or operate heavy machinery? Speak with your healthcare provider.
 - Note: Risk of motor vehicle accidents is increased 3-5X with narcolepsy.
 - As a result, some people take a stimulant before driving, drive only for short periods, or not drive at all.
- Educate parents, family and friends about narcolepsy.

Management: School and Workplace

School Accommodations for Narcolepsy

Consider the following accommodations for narcolepsy:

- Ensuring that educators learn about narcolepsy.
- Flexibility over absences. Be understanding that the student may arrive often late for school, or have absences due to narcolepsy symptoms.
- Designate an area where the student can go for both
 - Scheduled nap times, as well as
 - Nap times as needed in the case of a 'sleep attack'.
- Allow the student to leave the classroom as needed.
- For any missed classes due to narcolepsy, have a way for the student to be provided with notes from other students.
- Workload accommodations. Being sensitive to the student's limited ability to maintain wakefulness. Limit or avoid homework in the evenings.
- Testing accommodations. Allowing for breaks during testing times. Keeping testing times short enough to minimize potential for excessive sleepiness to intrude upon wakefulness. Extra time for deadlines and writing tests.

For more information, please see the following classroom resources on narcolepsy
<https://narcolepsynetwork.org/resources/for-students/>

Workplace Accommodations

- Sedentary jobs that require sustained attention may be challenging.
- Stimulating jobs may be a better fit.
- Educate managers about narcolepsy.
- Workplace accommodations and career counselling suggestions include:
 - Avoid jobs requiring sustained optimal alertness such as driving or using heavy machinery.
 - Avoid rotating or long shift work or long work hours.
 - Have strategically timed daytime naps (10-30 minutes) in order to avoid unintentional sleep attacks.
 - Consider jobs that involve cognitive work with flexible hours.

Management: Medications

Most people with narcolepsy require medication treatment (Scammell, 2015).

Is there mild-to-moderate daytime sleepiness?

- Modafinil (Alertec, Provigil) 200-800 mg daily (Ramar, 2013)

- Advantages: Relatively low side-effect profile; low potential for abuse. Black box warning label because of potential for teratogenic effects and inactivation of hormonal birth control, so caution is warranted for use in reproductive age women
- Mechanism of action: Felt to improve wakefulness by reducing the reuptake of dopamine.

Is there still sleepiness?

- Stimulants
 - Examples
 - Methylphenidate (Ritalin) 10-100 mg daily (Ramar, 2013)
 - Dextroamphetamine (Dexedrine) 5-60 mg daily (Ramar, 2013)
 - Advantages: More potent than modafinil.
 - Disadvantage: Higher risk of side effects and diversion.
 - Mechanism of action: Improve wakefulness by blocking the reuptake and increasing the release of dopamine

Medication Table for Excessive Daytime Sleepiness

Medication	Dosage
Modafinil	Adolescents /adults: Start 100-200 mg morn and 100-200 mg noon Maximum: up to 300 mg bid
Methylphenidate	Adult: 10-30 mg twice daily; 20 mg SR every morning with additional 10-20 mg afternoon
Dextroamphetamine	Adult 5-30 mg twice daily; or 10 mg sustained release every morning with additional 10-20 mg every afternoon
Sodium oxybate (sodium salt of GHB)	2.25-4.5 g bedtime Additional 2.25-4.5 g given 2.5-4 hr later

For cataplexy

Consider low dose antidepressant such as

- Venlafaxine (Effexor) in morning
- Atomoxetine (Strattera) in morning
- Fluoxetine (Prozac) in morning
- Advantage: Easier to prescribe

Is there moderate to severe sleepiness or cataplexy?

- Sodium oxybate (sodium salt of gamma hydroxybutyrate, GHB) (Xyrem)
 - Advantage: Felt to be the most effective
 - Disadvantage: Unfortunately it has significant potential for side effects and thus requires special licensing privileges to prescribe.

Medication Table for Cataplexy

Medication	Dosage
Venlafaxine XR	Adult: 37.5-75 mg twice daily
Fluoxetine	Adult: 20-80 mg mornings
Clomipramine	Adult: 10-150 mg bedtime or each morning
Sodium oxybate (sodium salt of GHB)	2.25-4.5 g bedtime Additional 2.25-4.5 g given 2.5-4 hr later

Course

Those with untreated narcolepsy struggle with functioning at school, work and home. They are at a high risk of being fired or getting into motor vehicle accidents. As a result, they are at a high risk of developing stress, anxiety and depression.

Even when people see health professionals, they are often misdiagnosed or told they are lazy and inattentive, or that they have conditions such as epilepsy, substance use problems, attention deficit disorder, depression, anxiety or even schizophrenia. These stigmas can often continue to persist by friends, family and colleagues after diagnosis. They often struggle for an average of 10 or more years before symptoms are identified and diagnosed.

Case, Part 2

Jennifer is in her 20's and has extreme problems with sleepiness and fatigue that has caused her to lose jobs, and gets in the way of relationships. You suspect narcolepsy, confirm that she has all the classic symptoms.

You start her on medication treatment, and she responds well. The effects are life-altering. With the improved energy and ability to stay awake until the early evening, she is able to work again, and reconnect with old friends and activities. Her struggles are far from over, but nonetheless things are significantly improved from when they were at their worst.

For More Information

Canadian Resources

Canadian Sleep Society (CSS)

<https://css-scs.ca>

Narcolepsy Canada

www.narcolepsycanada.ca

Narcolepsy Awareness Programs and Services

<https://www.facebook.com/pg/narcolepsycanada.ca/posts/>

American Resources

Narcolepsy Network

<http://www.narcolepsynetwork.org/>

National Sleep Foundation

<http://www.sleepfoundation.org/>

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Disclaimer

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