

### Excessive Daytime Sleepiness in Children

- ☞ 15% of young children with EDS (Bixler 2011)
- ☞ 68% of high school students report sleepiness (Gibson ES 2006)
  - ☞ Most sleepy between 8-10am
  - ☞ Mostly from sleep deprivation
  - ☞ Directly impacts the school performance
- ☞ EDS can present as irritability, inattentiveness and decreased school performance in children

Bixler 2011

### Causes of Sleepiness

- ☞ Sleep Restriction, Sleep Hygiene, Circadian misalignment, and Delayed Sleep Phase Syndrome
- ☞ Disrupted sleep due to OSA
- ☞ Depression/Anxiety
- ☞ Medication effect
- ☞ Narcolepsy
- ☞ Disrupted sleep due to PLMD

### Sleep Restriction

- ☞ Genetically hardwired INDIVIDUAL homeostatic sleep needs (usually 7-9 h)
- ☞ Sleep needs CANNOT be "trained"
- ☞ Adolescents are considered to need about an hour extra of sleep compared to adults
- ☞ Pressure on adolescent sleep time
  - ☞ Study/ activity time
  - ☞ Screen time
  - ☞ Peer pressure

### Effects of Sleep Restriction

- ☞ Acute Sleep Restriction
- ☞ Chronic Sleep Restriction

### Effect of Acute Sleep Restriction on Cognitive Throughput

Time since waking (h)	Cognitive throughput Deviation from mean (%)
0	0
10	-5
20	-10
30	-15
40	-20
50	-25

- 48 hours of wakefulness
- Simple 4-minute addition test

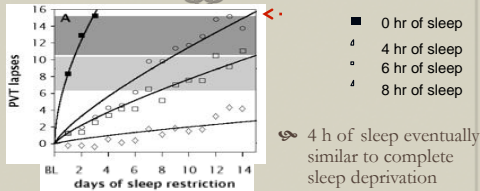
Sleep 22(suppl.):S94-S95, Jun. 1999

### Study of Chronic Sleep Restriction

- ☞ Assessed functioning after 4 and 6 h of daily sleep for 14 days in 48 adult volunteers
- ☞ Referenced to
  - ☞ 3 days of no sleep (worst case scenario)
  - ☞ 8 hours of daily sleep for 14 days (best case)
- ☞ Vigilance test, Digit symbol substitution, Addition Subtraction task, Subjective sleepiness scale

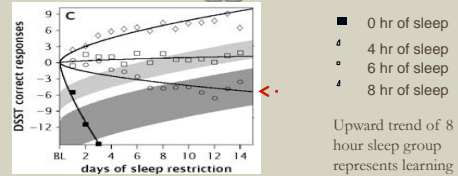
SLEEP, Vol. 26, No. 2, 2003

### Psychomotor Vigilance Test Lapses



4 h of sleep eventually similar to complete sleep deprivation

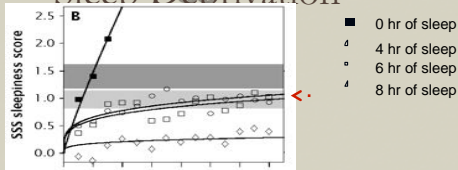
### DSST with Sleep Restriction



Downward movement indicates poorer performance; 6 h sleep stabilizes, 4 h does not

Upward trend of 8 hour sleep group represents learning effect

### Subjective Sleepiness with Sleep Deprivation



Sensation of sleepiness plateaus to level of one day of sleep loss

### Sleepiness and Performance are affected Differentially

- Unlike performance measures, **sleepiness ratings appeared to show adaptation** to chronic partial sleep deprivation
- Thus, subjects did not feel additional sleepiness that might inform them of deteriorated alertness
- May explain why sleep restriction is widely practiced

### Mechanisms of Phase Delay in Adolescents

- Reduced sleep pressure in adolescents
- Longer cycle time in adolescents in response to light
- Reduced response to light in morning (advance), greater response in evening (delay)
- Delayed recovery from phase shift

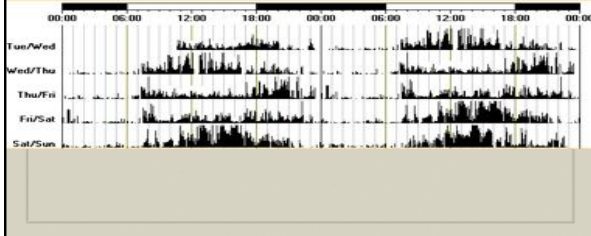
Dev Neurosci 2009;31:276-284

### Weekend Schedule

- Sleeping late on weekends, particularly with bright light exposure and waking up late can phase shift the internal clock
- Monday has a combination of sleep restriction and delayed sleep phase
- Naps likely as a result
- Entrainment back to regular schedule takes 1-3 days



## Actigraphy Sample



## Treatment of DSPS

- ☞ Light therapy
- ☞ Melatonin Therapy
- ☞ Chronotherapy
- ☞ General measures for sleep hygiene

## General Measures

- ☞ These are applicable to adolescents in general including
  - ☞ caffeine intake
  - ☞ limiting naps
  - ☞ sleep wake timing
  - ☞ sleep hygiene measures

## Minimize arousals in sleep setting

- ☞ Keep clock face turned away
- ☞ Avoid heavy meal 3 h before bedtime
- ☞ Keep room dark, quiet, well ventilated, and at a comfortable temperature
- ☞ Ear plugs/ eye shades may be beneficial
- ☞ Do not leave TV/ radio on

## Sleep Hygiene

- ☞ Wind down 1 hour before sleep time
- ☞ Avoid strenuous exercise after 6 pm
- ☞ Use a bedtime ritual
- ☞ No TV/ cell phone/ music gadgets/ computer in the bedroom
- ☞ Avoid unfamiliar sleep environments
- ☞ Bedroom for sleep only

## Sleep in Depression

- ☞ Sleep difficulties can -> depression symptoms and vice versa
- ☞ May have difficulty falling asleep
- ☞ May have multiple arousals
- ☞ Early morning awakening
- ☞ Poor sleep quality can lead to daytime tiredness and sleepiness
- ☞ Sleep hygiene and cognitive behavioral therapy can improve sleep quality

## Anxiety and Sleep

- ☞ Similar to depression, anxiety can lead to
  - ☞ Difficulty falling asleep
  - ☞ Difficulty maintaining sleep
  - ☞ Early morning arousals
- ☞ Screening for high stress- exams, school, family life
- ☞ Management of anxiety and behavioral therapy can improve sleep quality
- ☞ Again, managing expectations helps

THANK YOU FOR YOUR  
ATTENTION!

## Narcolepsy and MSLT in Children

## Outline

- ☞ Symptoms of narcolepsy
  - ☞ Case scenario
  - ☞ Secondary narcolepsy
- ☞ Diagnosis of narcolepsy in children
  - ☞ Delay in diagnosis
  - ☞ MSLT
- ☞ Treatment of Narcolepsy

## Case 1

- ☞ 5 yrs old female with excessive sleepiness and learning problems in school
- ☞ Mother describes the child as 'clumsy'
  - Excessive sleepiness never perceived as a problem until the learning difficulty was noted in school
  - Mother described herself as fortunate because the child slept so easily despite the fact that the child slept at inappropriate times (play and meal time)
  - Episodes of collapsing to floor abruptly with laughter
  - Also noted to have jaw drops
  - Also noted to have excessive weight gain
  - Child often described dreams of 'dinosaurs coming to her room'

Clinical Pediatrics 2002

## Case 1 continued

- The patient was evaluated by multiple physicians and was diagnosed with
  - ADHD
  - Hypothyroidism
  - 'jaw problems'
- Evaluated by sleep physician at age 6
  - PSG: Short sleep latency
  - MSLT: mean sleep latency: 2.8 minutes, 2 SOREM
- Child treated with methylphenidate and scheduled naps at school
- Improved quality of life and school performance
- Excessive weight gain and premature puberty (age 7)

## Case 2

- ☞ 12 yrs old male with progressive daytime sleepiness
  - ☞ Started napping during the day
  - ☞ Could not function well in school
  - ☞ Episodic muscle weakness, ptosis, dysarthria
  - ☞ Feeling of paralysis while playing videogame
  - ☞ Fell to the ground for few seconds without clear stimulus

Marcus 2010

## Case 2 continued


- ☞ Diagnosed with conversion disorder
  - ☞ Secondary to parental divorce
- ☞ Over the next one year
  - ☞ Visited several hospitals
  - ☞ Diagnosed with depression/ADHD
- ☞ Sleep center visit at age 13
  - ☞ Mean sleep latency 4.3 minutes, SOREM 2/4
  - ☞ HLA DQB1\*0602 positive, CSF hypocretin 31.7pg/ml
- ☞ Treated with modafinil and venlafaxine
- ☞ Started functioning better, symptoms well controlled

## Narcolepsy

- ☞ Focal neurodegenerative disease with genetic and autoimmune etiology involving the hypocretin (orexin) pathway
- ☞ Characterized by abnormal regulation of sleep wake with increased penetration of rapid eye movement sleep (REM sleep)
- ☞ Types
  - ☞ Narcolepsy with cataplexy
  - ☞ Narcolepsy without cataplexy
  - ☞ Secondary Narcolepsy

## Pediatric Narcolepsy

- ☞ Incidence 0.02-0.05%
- ☞ Affects males and females equally
- ☞ Reported across all ethnic groups
- ☞ Up to 50% of adult cases report symptom onset before age 15



Handbook of clinical neurology 2013

## Presenting symptoms in Pediatric Narcolepsy

- ☞ Excessive daytime sleepiness (EDS)
- ☞ Cataplexy
- ☞ Sleep paralysis
- ☞ Hypnagogic hallucinations
- ☞ Other issues
  - ☞ Obesity
  - ☞ Precocious puberty
  - ☞ Psychosocial issues

## EDS how do we measure?

- ☞ Epworth sleepiness scale (ESS)
  - ☞ Widely used, - Not applicable in young children
- ☞ Stanford sleepiness scale
  - ☞ Evaluates feeling of sleepiness at that moment
- ☞ Pediatric sleep questionnaire
  - ☞ Subset of 4 questions on sleepiness
- ☞ Pediatric daytime sleepiness scale
  - ☞ **Pediatricians should ask for**
    - ☞ Amount of sleep at night, falling asleep in school, falling asleep at inappropriate times

## Cataplexy

- ☞ Abrupt partial or complete loss of muscle tone
  - ☞ Does not involve loss of consciousness or amnesia
  - ☞ Complete recovery within few minutes
  - ☞ Bilateral, sometimes unilateral
  - ☞ Provoked by strong emotion, usually laughter
    - ☞ Can be spontaneous (~60%)
  - ☞ Often misdiagnosed as
    - ☞ Child being lazy, clumsy
    - ☞ Staring spells/seizures
    - ☞ Jaw problems

## Sleep Paralysis

- ☞ Episodic loss of voluntary muscle control usually occurring during sleep wake transition
- ☞ Attacks last for several minutes
- ☞ Often accompanied by sleep hallucinations
- ☞ Reported in 20-60% of the cases
  - ☞ Difficult to elicit this history in young children

Aran 2010, Okun M L 2001, Nevsimalova 2013

## Sleep Hallucinations

- ☞ May be seen in up to 60% of the children
- ☞ Vivid dreams, usually frightening
- ☞ Often occurs with sleep paralysis
- ☞ Children may report 'colored circles, images of animals/people'
- ☞ Confused with sleep terrors/nightmares/panic attacks
- ☞ Can occur even during naps


Aran 2010, Okun M L 2001, Nevsimalova 2013

## Pediatric Narcolepsy and Obesity

- ☞ Retrospective chart analysis of 51 narcoleptic children followed at Stanford (Aran 2010)
  - ☞ Significant weight gain (avg 4kgs) within 6 months of the diagnosis
  - ☞ ~50% pre-pubertal at diagnosis
  - ☞ Early puberty in those who gained more than 10kgs
- ☞ Chart analysis of 107 French children with Narcolepsy (Inocente 2013)
  - ☞ ~60% of narcoleptic children with overweight and obesity
  - ☞ Mostly seen in children with early onset narcolepsy
  - ☞ Increased sleep disturbance and sleep apnea in obese group

## Psychosocial and cognitive issues

- ☞ Psychosocial problems and cognitive impairment common in narcolepsy
  - ☞ Hypocretin system also involved in monitoring emotions and cognitive function
- ☞ Psychosocial issues
  - ☞ Depression is common
  - ☞ Behavioral changes
    - ☞ Conflicts with the family
    - ☞ Problems at school
- ☞ Cognitive impairment
  - ☞ Some impairment in executive function, emotional learning and reward expectancy
  - ☞ Not studied in children



Narcolepsy: The Reality

Nevsimalova 2009

## Adolescent narcolepsy

- ☞ Common
- ☞ Up to 50% adult cases- started in adolescence
- ☞ Excessive sleepiness common in teens
  - ☞ Delayed sleep phase
  - ☞ Inadequate sleep hygiene
  - ☞ Denial about daytime sleepiness
- ☞ Depression/ADHD common misdiagnosis
- ☞ Stimulants over use?
  - ☞ Screening for sleep disorders
  - ☞ Awareness among primary physicians



## Childhood narcolepsy

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Common misdiagnosis

- ☞ Learning difficulties
- ☞ ADHD
- ☞ Clumsy/sloppy child

Sleepiness noted to be a problem at school than at home

Significant delay in diagnosis

Some may be masked/never diagnosed as the first line treatment for narcolepsy and ADHD are the same

- ☞ Screen for sleep disorders?
- ☞ Educating primary physicians?

## Secondary Narcolepsy

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- ☞ Relatively common in children
- ☞ Associated with
  - ☞ Brain tumors
  - ☞ Demyelination
  - ☞ Infection/encephalitis
  - ☞ Neiman pick disease
  - ☞ Prader willi syndrome
- ☞ Cataplexy common; status catalepticus
- ☞ Earlier age of onset (~6 yrs)
- ☞ Effective control of symptoms by conventional treatment

## Diagnosis of narcolepsy

Table 1  
Diagnostic criteria for narcolepsy as proposed by the International Classification of Sleep Disorders

1. Narcolepsy with cataplexy
  - A. Excessive daytime sleepiness almost daily for at least 3 months
  - B. Definite history of cataplexy
  - C. Diagnosis should be confirmed, whenever possible, by one of the following:
    1. PSG and MSLT; mean sleep latency should be <8 minutes and at least 2 SOREMPs
    2. CSF hypocretin level <110 pg/mL or 1/3 of mean normal controls
  - D. Hypersomnia is not better explained by another disorder or medication
2. Narcolepsy without cataplexy
  - A. Excessive daytime sleepiness almost daily for at least 3 months
  - B. Definite cataplexy is not present
  - C. Diagnosis must be confirmed by one of the PSG and MSLT; mean sleep latency should be <8 minutes and at least 2 SOREMPs
  - D. Hypersomnia is not better explained by another disorder or medication
3. Secondary narcolepsy (narcolepsy due to medical condition)
  - A. Excessive daytime sleepiness almost daily for at least 3 months
  - B. One of the following is present:
    1. Definite history of cataplexy
    2. If cataplexy is not present, diagnosis must be confirmed by PSG and MSLT; mean sleep latency should be <8 minutes and at least 2 SOREMPs
    3. CSF hypocretin level <110 pg/mL
  - C. Underlying medical or neurological condition accounts for the sleepiness
  - D. Hypersomnia is not better explained by another disorder or medication

Peterson 2008

## Age of onset- starts early on

Role for pediatrician

FIG. 1. Age at onset of narcolepsy, as reported by 83 consecutive adult patients.

Pediatrics, Yoss, 1960

## Multiple sleep latency test

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- ☞ The Multiple Sleep Latency Test (MSLT) is a validated objective measure of the ability or tendency to fall asleep
- ☞ The MSLT consists of five nap opportunities performed at two-hour intervals. The initial nap opportunity begins 1.5 to 3 hours after termination of the nocturnal recording

## MSLT in narcolepsy

- ☞ Polysomnography(PSG) should be performed during the major sleep period that precedes the nap testing
  - ☞ exclude other major sleep disorders that could contribute to sleepiness and to assure that the individual had sufficient sleep
  - ☞ no specific recommendations for sleep duration on the PSG preceding the MSLT in children
- ☞ PSG findings
  - ☞ SOREM
  - ☞ fragmented sleep
  - ☞ leg movements

Sleep 2012

## MSLT in narcolepsy

- ☞ MSLT has a sensitivity for diagnosing narcolepsy ranging from 79% to 100%
- ☞ Diagnostic criteria: Mean sleep onset latency < 8 min, and 2 Sleep onset REM (SOREM)
- ☞ Many children who had narcolepsy with cataplexy had mean sleep latencies < 5 minutes and more than 2 SOREMPs.
- ☞ MSLT can also be used to assess the response to treatment

**Your Multiple Sleep Latency Test (MSLT)**  
What to expect

1. Lighten up
2. Patient awake
3. Patient reading
4. Patient asleep
5. Patient awake
6. Patient reading
7. Patient asleep
8. Patient awake
9. Patient reading

Sleep 2012

## Other tests

- ☞ HLA DQB1 0602
  - ☞ Sensitivity highest in patients with narcolepsy and cataplexy
  - ☞ Frequently present in general population; limiting the utility as a diagnostic tool
- ☞ CSF hypocretin <100pg/ml
  - ☞ Can be used as a diagnostic tool in
    - ☞ Young children (<5 yrs)
    - ☞ Children with complex medical conditions/ on psychotropic medications
- ☞ CNS imaging
  - ☞ ? Secondary cases

# Treatment of Narcolepsy

## Behavioral therapy

- ☞ Educating patients, parents and teachers
  - ☞ Nature of the disorder
  - ☞ Importance of adequate sleep hygiene
  - ☞ Structured sleep
- ☞ Scheduled naps during the day
  - ☞ 20minute naps twice a day
- ☞ Narcolepsy support groups

Morgenthaler T I 2007; Rogers AE 2001

## Pharmacological Treatment

- ☞ No RCT'S done in children
- ☞ Efficacy and safety
  - ☞ mostly from adult trials and some
  - ☞ Chart review/case series in children
- ☞ Therapy is usually lifelong
- ☞ Treatment focused on
  - ☞ EDS
  - ☞ Cataplexy
- ☞ Careful monitoring for side effects

### Treatment of EDS: Modafanil

- Non amphetamine wakefulness promoting agent
- Works via dopaminergic pathway
- Has been studied in children with ADHD
- Starting dose 100mg; can be titrated up to 200/400mg
- Advantages
  - ☞ Long half life; single morning dose is enough
  - ☞ Lack of dependency
- Side effects
  - ☞ Headache, nausea, dry mouth
  - ☞ Alternative form of contraception in women of childbearing age group

### Treatment of EDS: Methyphenidate

- ☞ CNS stimulant
  - ☞ Acts by blocking both dopamine and nor epinephrine re-uptake
  - ☞ Potent – first line in some countries
    - ☞ Side effects
      - ☞ Psychosis, arrythmia, anorexia, sudden death
    - ☞ Potential for dependence
    - ☞ Closely monitor
      - ☞ Heart rate, blood pressure, weight
  - ☞ Starting dose:0.3mg/kg/dose
    - ☞ Weekly titration depending on clinical response and side effects

### Treatment of cataplexy

- ☞ REM suppressing agents
  - ☞ Tricyclic antidepressants
  - ☞ Selective serotonin reuptake inhibitors
  - ☞ Norepinephrine reuptake inhibitors
- ☞ Gamma hydroxybutyrate (GHB)
  - ☞ Metabolite of GABA
  - ☞ Specifically binds to GABA-B and GHB receptors

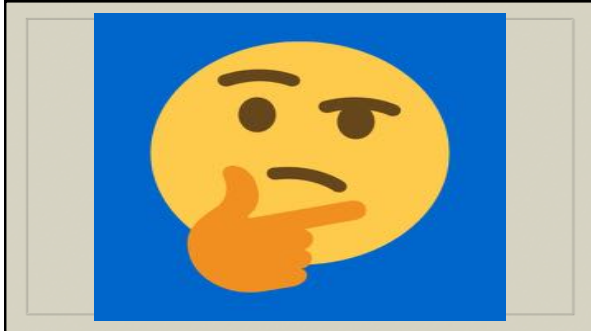
### Sodium oxybate use in children

- ☞ Dispensed as liquid
- ☞ Short half life
  - ☞ Need for 2 doses at night
- ☞ Side effects
  - ☞ Sedation, deep coma/death secondary to overdose
  - ☞ High abuse potential; dispensed by central pharmacy
- ☞ Retrospective chart review in children<sup>1</sup>
  - ☞ 15 children (3-15yrs), followed 3-90months, mean dose 5±2G
  - ☞ Significant improvement in EDS/cataplexy
  - ☞ Significant social/academic improvement
  - ☞ Side effects (40%):tremor, blurring of vision, sustained improvement, no tolerance

<sup>1</sup>Kotagal 2011

THANK YOU FOR YOUR ATTENTION!

Restless Leg Syndrome [RLS]  
 Periodic Limb Movement Disorder [PLMD]



## Case History

- ☞ An eight-year-old boy with attention deficit hyperactivity disorder (ADHD) presents with a one-year history of intermittent 'tingling' in his legs, when sitting in school, which is relieved by walking but is now interfering with his ability to fall asleep and stay asleep. His mother's symptoms meet adult criteria for restless legs syndrome (RLS), and his, for 'probable RLS'. He eats little red meat. His ferritin level is 15  $\mu\text{g/L}$ , transferrin saturation 0.13, and his total iron-binding capacity (TIBC) and complete blood count (CBC) are normal.

## RLS & PLMD

- ☞ PLMS, often rhythmic extension of the big toe and ankle dorsiflexion, occur at intervals of 20 s to 40 s and may be associated with arousal.
- ☞ Not all children with RLS have PLMS.
- ☞ RLS is diagnosed by history and PLMS by overnight sleep study (polysomnography [PSG]).
- ☞ One-third of adults with RLS are affected in childhood.
- ☞ Genetic, Central nervous system iron deficiency and dopaminergic dysfunction

## RLS in Children

- ☞ Limited epidemiology
- ☞ Reported at 1.3 – 2% of school age children
- ☞ Criteria – Adult 4 features
  - ☞ Child Modified criteria: Definite, Probable, Possible
- ☞ PLMD Criteria
- ☞ Diagnostic awareness
- ☞ Treatment options

Dosman 2012

## Definite Criteria

**Diagnostic criteria for definite restless legs syndrome (RLS)**

**Criteria for the diagnosis of definite RLS in children:**

- 1) The child meets all four essential adult criteria for RLS (below) AND
- 2) The child relates a description in his or her own words that is consistent with leg discomfort. (The child may use terms such as 'twitches', 'tolls', 'spiders', 'boo-boos', 'want to run and a lot of energy in my legs to describe symptoms. Age-appropriate descriptors are encouraged).

**OR**

- 1) The child meets all four essential adult criteria for RLS AND
- 2) Two of the three following supportive criteria are present:
  - a) Sleep disturbance for age
  - b) A biological parent or sibling has definite RLS
  - c) The child has a polysomnographically documented periodic limb movement index of 5 or more per hour of sleep.

**Essential adult criteria**

- 1) An urge to move the legs, usually accompanied or caused by uncomfortable and unpleasant sensations in the legs (sometimes the urge to move is present without the uncomfortable sensations and sometimes the arms or other body parts are involved in addition to the legs).
- 2) The urge to move or unpleasant sensations begin or worsen during periods of rest or inactivity such as lying or sitting.
- 3) The urge to move or unpleasant sensations are partially or totally relieved by movement, such as walking or stretching, at least as long as the activity continues.
- 4) The urge to move or unpleasant sensations are worse in the evening or night than during the day or only occur in the evening or night (when symptoms are very severe, the worsening at night may not be noticeable but must have been previously greater).

Dosman 2012

## Probable & Possible

**Diagnostic criteria for probable and possible restless legs syndrome (RLS) in children**

**Criteria for the diagnosis of probable RLS**

- 1) The child meets all essential adult criteria for RLS, except criterion 4 (ie, the urge to move or sensations are worse in the evening or at night than during the day) AND
- 2) The child has a biological parent or sibling with definite RLS

**OR**

- 1) The child is observed to have behavioural manifestations of lower extremity discomfort when sitting or lying, accompanied by motor movement of the affected limbs. The discomfort has characteristics of adult criteria 2, 3 and 4 (ie, is worse during rest and inactivity, relieved by movement, and worse during the evening and at night) AND
- 2) The child has a biological parent or sibling with definite RLS\*

**Criteria for the diagnosis of possible RLS**

- 1) The child has periodic limb movement disorder (PLMD) AND
- 2) The child has a biological parent or sibling with definite RLS, but the child does not meet definite or probable childhood RLS definitions

Dosman 2012

## PLMD

### Criteria for the diagnosis of PLMD in children

- 1) Polysomnography shows a periodic limb movement index of 5 or more per hour of sleep. The leg movements are 0.5 s to 5 s in duration, occur at intervals of 5 s to 90 s, occur in groups of 4 or more, and have an amplitude of 25% or more of toe dorsiflexion during calibration AND
- 2) Clinical sleep disturbance for age must be evident as manifested by sleep onset problems, sleep maintenance problems or excessive sleepiness AND
- 3) The leg movements cannot be accounted for by sleep disordered breathing (ie, the movements are independent of any abnormal respiratory events) or medication effect (eg anti-depressant medication)

Dosman 2012

## Treatment

- ☞ Variable evidence for Iron
- ☞ Widely used
- ☞ Ferritin less than 50 worth treating
- ☞ Dopaminergic medication – very limited paediatric literature
  - ☞ Used in centres with research base, experimental

## Non Pharmacological Mgmt

### Nonpharmacological paediatric restless legs syndrome (RLS) treatment

#### Sleep hygiene

Consistent and age-appropriate bedtime routine  
Consistent and age-appropriate sleep schedule (weekdays and weekends)  
Sufficient duration of nighttime sleep

Caffeine elimination (chocolate, carbonated beverages)

Restriction of other known RLS causes/exacerbators: selective serotonin reuptake inhibitors, selective norepinephrine-serotonin reuptake inhibitors, tricyclic antidepressants, antipsychotics, antihistamines, cold/sinus preparations, antiemetics, nicotine, alcohol

#### Behavioural strategies

Progressive muscle relaxation, card games  
Remaining out of the bed until ready to fall asleep  
Regular exercise several hours before bedtime (to increase sleep)  
Walking, stretching  
Massage

Hot or cold packs to help pain associated with RLS

Dosman 2012

THANK YOU FOR YOUR  
ATTENTION!