ADHD: Current Update
Co-morbidity and Treatment Strategies
CADDRA Guidelines

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CADDRA
CANADIAN ADHD/ADD RESOURCE ALLIANCE
## Disclosure Statement

### Pharmaceutical Company Sponsorships

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*This talk sponsored by Shire Biochem and Janssen-Ortho*
A national organization to advocate for all ADHD patients

- physician lead but will soon include key stakeholders

- involved in research, training and advocacy

- produced the Canadian ADHD Practice Guidelines (CAP-Guidelines)
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<tr>
<th>Name</th>
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<tr>
<td>Sarah Shea</td>
<td>Atlantic</td>
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<td>Umesh Jain</td>
<td>Ontario</td>
<td>Chair/Admin</td>
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<td>Lily Hechtman</td>
<td>Quebec</td>
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<td>Annick Vincent</td>
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<td>Derryck Smith</td>
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<td>Declan Quinn</td>
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<td>Margaret Weiss</td>
<td>BC</td>
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Material will be downloadable
www.caddra.org
www.caddra.ca

Material can be obtained from industry reps
Direct distribution to physicians
(only cost is Postage and Handling)
Objectives:

To review the diagnosis of Attention-Deficit / Hyperactivity Disorder (ADHD) using the CADDRA Guidelines

To review new treatment strategies
ADHD: Timeline of Definitions

1902: First Description of ADHD by Still
1930: Minimal Brain Damage
1937: Hyperkinetic Reaction of Childhood (DSM-II)
1950: Efficacy of Amphetamine
1968: Hyperactive Child Syndrome
1970: Attention Deficit Disorder ± Hyperactivity (DSM-III)
1980: Attention Deficit/Hyperactivity Disorder (DSM-III-R)
1987: Adult ADHD Studied
1994: Attention Deficit/Hyperactivity Disorder (DSM-IV)
Media Hype and Confusion

NewswEEK
Ritalin
Are We Overmedicating Our Kids?
Myths and Facts

ADHD is only a childhood disorder and applies only to boys
It is only found in Western countries
It is a behavioral disorder
It reflects inadequate school funding and that kids are over diagnosed
The medical agenda is being pushed by drug companies

ADHD is lifespan disorder and many girls with inattention are not identified
ICD-10 Criteria used elsewhere
ADHD is a worldwide phenomena
It is a medical disorder that affects learning
The prevalence rates are 5-9% though incidence has increased
The MTA study was NIMH funded
Prevalence Rates

Prevalence

- ~8% of school age children\(^1\)
- ~50% persistence into adulthood\(^2\)
- 4.4% of adults meet full criteria for persistent childhood-onset ADHD with significant impairment and comorbidity\(^3\)

Worldwide Rates of ADHD

(Faraone et al. World Psych:2003)

Prevalence of ADHD (%)

NY, MI, WI
N. Carolina
Virginia
Missouri
Oregon
Minnesota
Tennessee
Iowa
Pittsburgh
New York City
Puerto Rico

Spain
New Zealand
Canada
Ireland
United Kingdom
Israel
Switzerland
Netherlands/Belgium
Germany
Ukraine
Brazil
Japan
New Zealand
Netherlands
China
Southeast Asia

Prevalence of ADHD (%)
ADHD is impairing

Coping strategies may limit impairment if the person can find a suitable niche.

Impairment can be found in many domains.

“Patients do not meet their potential”
## Potential Consequences of Untreated ADHD Throughout the Day

<table>
<thead>
<tr>
<th>Time</th>
<th>Work</th>
<th>Outside Work/Home</th>
<th>Home</th>
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<tbody>
<tr>
<td>7:00 AM</td>
<td>Late for Work</td>
<td>Poor Driving Habits</td>
<td>Significant Marital Problems</td>
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<tr>
<td></td>
<td>Delays Projects Until Deadlines Are Imminent</td>
<td>Frequent Traffic Accidents/Violations</td>
<td>Parenting and Child Care/Management Difficulties</td>
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<tr>
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<td>Forgetful of Things to Be Done</td>
<td>Low Self-Esteem</td>
<td>More Chaotic Family Routines</td>
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<tr>
<td></td>
<td>Poor Organization</td>
<td>Substance Abuse</td>
<td>Poor Financial Management</td>
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<tr>
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<td>Easily Bored by Tedious Tasks</td>
<td>Fewer Friends</td>
<td>Poor Housekeeping</td>
</tr>
<tr>
<td></td>
<td>Impulsive Job Changes</td>
<td>Criminal Activities</td>
<td>Trouble Sustaining Intimate Relationships</td>
</tr>
</tbody>
</table>

Long-term Educational Impairment

Did not graduate college
Drop-out
Expulsion
Suspension
Grade retention

Change Jobs More Often

More Likely to Be Fired

Odds Ratio

Barkley RA. J Clin Psychiatry. 2002;63(suppl 12):10-15
ADHD, Predominantly Combined Subtype (ADHD-C) >50%

ADHD, Predominantly Inattentive Subtype (ADHD-I) 35%

ADHD, Predominantly Hyperactive-Impulsive Subtype (ADHD-HI) <10%
Assessment Algorithm for ADHD

- Screening
  - DSM-TR + SNAP Questionnaires (ensure referral for psychometrist)

- Documentation using the CADDRA Child and Adolescent Template
- Inclusion Strategies also include:
  - Family History
  - Childhood History (also school report cards and other assessments)
- Exclusion Strategies
  - CADDRA Co-morbidity Scales (Turgay) or Checkmate Plus

- Impairment Scales
  - WFIRS – review domains of functioning

- CADDRA Feedback Form
  - Presented to family so they know how the diagnosis was made
ADHD etiology: No simple solutions

Behavioral
- hyperactivity
- impulsivity

Social
- isolation
- rejection
- asocial
- antisocial

Cognitive
- Inattention
- Concentration
- Memory

Emotional
- Temper
- Affect regulation
- Mood problems
Biological Evidence for ADHD

PET Studies
Cognitive Data
Neuro-chemical evidence
Genetic Data
Prepubescent Growth Spurt in Cortex
(thickens just before puberty, then thins)

Aggregate of 52 MRI scans of normal kids scanned @ 2 yr intervals
Cortex thickness peaks at
11 yo in females
12.5 in males
Then prunes for
More efficient circuits

[View of right orbital lateral cortex; blue is thinner]
Positron Emission Tomography (PET) studies show that methylphenidate acts predominantly in the striatum of the human brain where it binds to DA transporters.

Volkow et al. J Atten Disord 2002
Ritalin improves glucose consumption in the brain.

Increased consumption with Ritalin

ADHD: Decreased consumption
Average genetic contribution of ADHD based on twin studies

The Dopamine Connection

Convincing clinical evidence of stimulant responsiveness (possible self medication with THC and cocaine)

Cognitive changes that show normalization of inhibitory control (Stopsignal paradigm test) and alteration in blood flow on PET scanning

Genetic findings point to possible dopamine factors
Dopamine Neurotransmission

Enhances signal
Improves attention

- Focus
- On-task behavior
- On-task cognition

Dopamine

Noradrenaline Connection

Part of the same catecholamine pathway

If the only way to keep your brain on is to create crisis, activation of noradrenaline

Alteration in arousal

Helped with noradrenaline based medication
Noradrenaline Neurotransmission

- Dampens noise
- Executive operations
- Increases inhibition

Mechanism of Action - NA Agonists

1. Data on File: Eli Lilly and Company
Mechanism of Action of Stimulants

Amphetamine blocks reuptake

Methylphenidate blocks reuptake

Presynaptic Neuron

Cytoplasmic DA

Storage vesicle

DA Transporter

Synapse

This trial randomized 579 children aged 7-9 years to one of four treatment arms over 14 months:

1. Monthly management of medication treatment with supportive care
2. Intensive behavioural treatment
3. Medication plus supportive care and intensive behavioural treatment
4. Usual community care (most cases with medication, not closely monitored)
5. Follow up for ten years

MTA group, Arch Gen Psychiatry 1999;56:1073-1086
Parent SNAP-Hyp/Impulsive

Time x Tx: F=21.5, p<.0001
Site x Tx: F=1.3, ns
Site: F=4.4, p<.0006

Comb, MedMgt > Beh, CC
Teacher SNAP-ODD/Aggressive

Time x Tx: $F=6.5$, $p<.0003$
Site x Tx: $F=1.2$, ns
Site: $F=4.2$, $p<.001$

Comb, MedMgt $>$ CC
Long acting agents will be first line

- Across the lifespan but particularly for adolescents and adults

Short acting agents will be considered adjuvant treatments in the first line
**The Need for Once-Daily Dosage Options**

*Extended medication coverage needed*
- After school, extracurricular activities
- Social interactions
- Homework hours

*Problems with in-school dosing*
- Privacy issues
  - Ridicule by peers; decreased self-esteem
- Storage of controlled medications
  - Security; potential for diversion
ADHD Medications (in alphabetical order)

CADDRA guidelines
- information downloadable
- useful for parents and adolescents

SE suggestions also listed
Adderall XR is registered in the US patent and trademark office. Slide provided by Shire Biochem.
Adderall XR™ Profile

- 50% at the beginning
- 8-12 hr duration
- Sprinkle formulation
- Efficacy and safety established
- #1 selling ADHD medication worldwide
- Multiple doses make it easy to titrate
- Broad indications - all age groups in the US
Biphentin® Profile

40/60 delivery system
Controlled release patented technology
Seven doses – easy exchange to t.i.d. dosing
Sprinkle format
Made in Canada and available only in Canada
10-12 hour duration
Active ingredient well established efficacy and safety
Indicated in all age groups (including adults)
Concerta ™ Profile

22% delivery then 78% release

8-12 hr duration

Few formulations (4 doses) but easy to titrate

5 tid = 18, 10 tid = 36, 15 tid = 54

Covered by Ontario and Quebec limited access

Established efficacy and safety
24 hour coverage
Samples available
Maintains a blood level and dosing can be adjusted
Limited Access Coverage in Ontario and in PQ
Multiple doses
Cost no different than most antidepressants
Non-controlled substance
Side effects limited with slower titration

Slide provided by Eli Lilly. Strattera® is a registered product by Eli Lilly.
Syndrome of ADD Impairments is involved in most disorders

Disorders of Executive Functions
- Developed or Acquired

Language & Learning
- Exp Lang
- Recep Lang
- Reading LD
- Math LD
- Written Exp LD

Arousal & Motivation
- Dysth/Depression
- Anxiety
- PTSD
- Bipolar
- OCD
- Substance Abuse

Social-Emotional Regulation
- Asperger's
- Autism/PDD
- ODD
- Conduct
- Tourette's

Impairments of EF involved in all of these

Used by permission, Tom Brown, CADDRA meeting June 2006
ADHD Co-morbidity

- ADHD: 49%
- Conduct Disorder: 7%
- Anxiety Disorder: 11%
- Depression: 11%

- 6% overlap between ADHD and Conduct Disorder
- 5% overlap between Conduct Disorder and Anxiety Disorder
- 4% overlap between Anxiety Disorder and Depression
- 9% overlap between ADHD and Depression

ADHD Resource Alliance
MDD=major depressive disorder. LD=learning disability. ASP=antisocial personality disorder.
Oppositional Defiant Disorder

Driven by the ADHD
Reflective of environmental insecurity
Cultural

If driven by ADHD, treatment of ADHD will lessen the ODD symptoms
Holistic Interventions

The medications are there to facilitate the other interventions

- Behavioral
- Psychological
- School- Educational
- Social
CONTACT INFO

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