International guidelines for assessment and management of ADHD

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Disclosure

Presented at professional meetings sponsored by the following pharmaceutical companies:

- Eli Lilly
- Novartis
- Janssen Cilag
- Merck Sharp and Dohme

Epidemiology and Clinical Course

North Carolina	10% ADHD, 7% Medication
Rhode Island	12% referred for evaluation ADHD, 6% Medication
Rochester MN	7.5% cumulative incidence ADHD
US Health IV survey	6.7% prevalence ADHD
CDC National survey	7.8% lifetime diagnosis ADHD, 4.3% Medication
Longitudinal studies	60-85% children with ADHD -> teenage years 40% children with ADHD still ADHD 18-20 years Prevalence ADHD in adults 4.4%

Biological contributions to ADHD

- Wilcutt 2005 meta-analysis 83 studies, >6000 subjects
  - Patients with ADHD have impairments in executive functioning domains of response inhibition, vigilance, working memory, and planning
- Farraone 2005 meta-analysis 20 independent twin studies
  - Heredibility of ADHD: 76% of symptoms explained by genetic factors
  - Seven genes showed statistically significant evidence of association with ADHD: dopamine 4 and 5 receptors, dopamine transporter, dopamine beta hydroxylase, serotonin transporter, serotonin 1B receptor, synaptosomal associated protein 25 gene
- Non-genetic biological associations
  - Perinatal stress, low birthweight, traumatic brain injury, maternal smoking during pregnancy, severe early deprivation

Comorbidities

Oppositional Defiant Disorder	54-84%
Conduct Disorder	25%
Substance Abuse Disorders	10%
Learning and Language disorders	25-35%
Anxiety Disorders	30%
Depressive Disorders	0-33%
Bipolar II	15%
Pervasive Developmental Disorders	0-15%

Recommendation 1. Screening for ADHD should be part of every patients mental health assessment

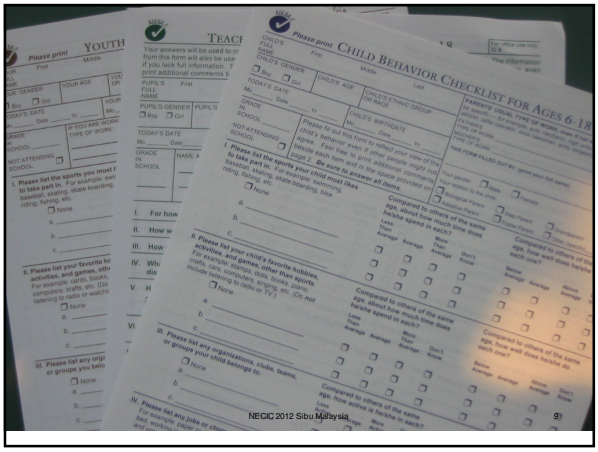
- Ask questions about inattention, impulsivity, hyperactivity and whether symptoms cause impairment
- Use standardised rating scales to supplement clinical questioning

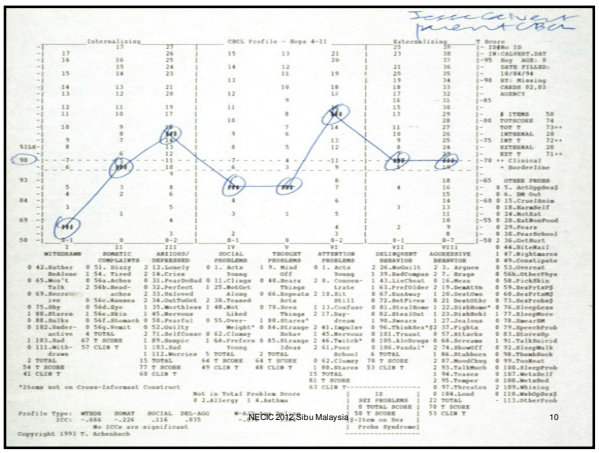
Recommendation 2. Evaluation of the preschooler, child or adolescent should consist of clinical interviews with the parent and patient, information from preschool or school, assessment for comorbid psychiatric disorders and review of medical social and family histories

- Ask about each of 18 ADHD symptoms, duration, severity, frequency, age of onset
- In which settings impairment occurs (DSM IV requires impairment in at least two settings (home school or job). Clinical consensus indicates that severe impairment in one setting warrants treatment
- Screen for comorbid disorders ODD, CD, depression, mania, anxiety, tics, substance abuse, psychosis, learning difficulties
- Best done with standardised behaviour rating scales

Rating scales

- General behaviour rating scales
  - Achenbach Child Behaviour Checklists (CBCL)
  - Behaviour Assessment System for Children (BASC)
- Diagnosis specific rating scales
  - ADHD rating scale IV (DuPaul)
  - Conners Parent and Teacher rating scales
  - SNAP IV parent and teacher rating scale (Swanson)
  - SWAN rating scale
  - Daily Parent Rating of Evening & Morning Behaviour (Lilly)
  - School Situations Questionnaire (Barkley)




CBCL Profile - Boys 4-11
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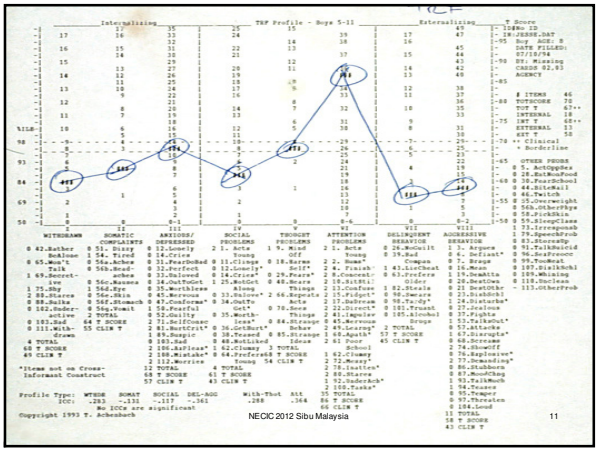
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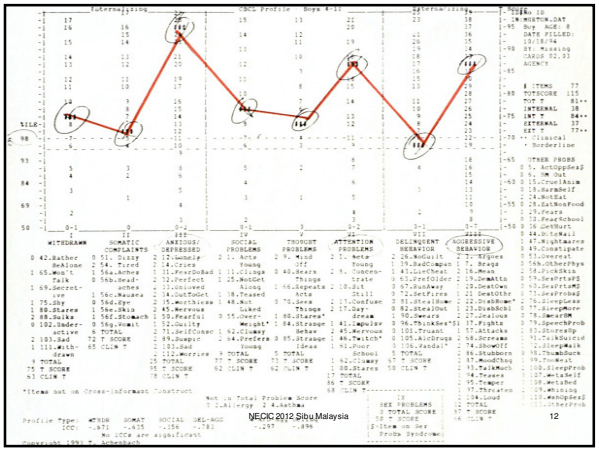
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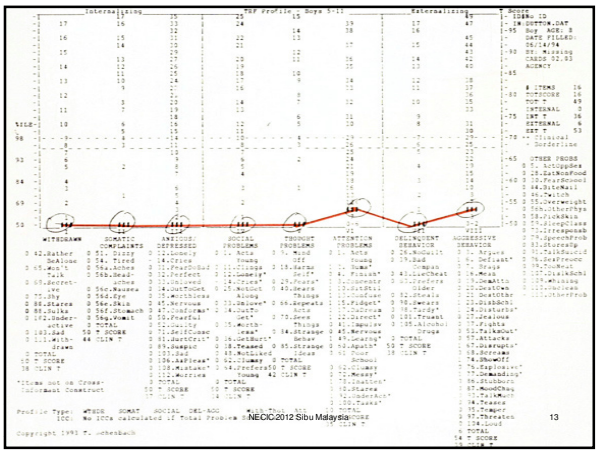

ADHD rating scales IV

- Simple list of DSM symptom criteria
- Parent, Teacher and Self-Report forms
- Odd numbered items – Inattentive
- Even numbered items – Hyperactive/impulsive
- Four point scale
  - never
  - sometimes
  - often
  - very often
- symptoms often/very often = positive
- symptoms never/sometimes = negative
- > 6/9 items positive for inattention and / or hyperactivity/impulsivity = statistically deviant
- Parent AND Teacher ratings deviant = disorder

Conners Rating Scales - revised

- Oldest and best known ADHD scales
- Ages 3-17
- 28 items marked as
  - Not true
  - Just a little true
  - Pretty much true
  - Very much true
- Scoring in 4 subscales
  - Oppositional
  - Cognitive problems / inattention
  - Hyperactivity
  - ADHD index
- Norm referenced, hand scored
- T score 70 = 98th%, T score 65 = 93rd %

SWAN Rating scale

- Adaptation of SNAP with different scoring system. Items marked:
  - +3. Far below average
  - +2. Below average
  - +1. Slightly below average
  - 0. Average
  - -1. Slightly above average
  - -2. Above average
  - -3. Far above average
- Better psychometric properties, less likely to over-identify children with ADHD
- Mean score > 2 = > 98th percentile

Recommendation 3. If the patient's medical history is unremarkable, laboratory or neurological testing is not indicated

- Very few medical conditions masquerade as ADHD
  - Traumatic brain injury
  - Encephalopathies
  - Hyperthyroidism
  - Lead toxicity
  - Foetal alcohol syndrome
- Don't do cranial MRI, EEG, SPECT or PET

Recommendation 4. Psychological and neuropsychological tests are not mandatory for the diagnosis of ADHD but should be performed if the patients history suggests low general cognitive ability or low academic achievement relative to ability

- Academic impairment is commonly due to the ADHD itself
- In most cases treat the ADHD and then determine whether the academic problems begin to resolve
- If no clear improvement in 2-3 months then psychological testing is indicated
- Standard IQ tests, neuropsychological tests, academic achievement tests, speech and language tests

Recommendation 5. Evaluate the patient with ADHD for the presence of cormorbid psychiatric disorders

- Does patient meet criteria for separate comorbid disorder?
  - If full DSM IV criteria met for a second disorder the clinician should generally assume the patient has two or more disorders and develop a treatment plan to address each comorbid disorder
  - ODD/CD almost always present with ADHD concurrently in clinic samples
  - Onset of depressive disorder usually occurs several years after the onset of ADHD
  - Anxiety disorders have an earlier onset concurrent with the ADHD
  - Comorbid Bipolar II should be considered in patients with severe mood lability/elation/irritability, thought disorder, decreased sleep, severe aggression (affective storms)
- Is the comorbid disorder the primary disorder?
- Do comorbid symptoms not meet criteria for a separate disorder but represent secondary symptoms stemming from the ADHD?

Recommendation 6. A well thought out and comprehensive treatment plan should be developed

- Pharmacologic and behavioural therapies
- Studies consistently support the superiority of stimulant over non-drug treatment.
- MTA study
  - Four treatment arms: medication alone, psychosocial treatment alone, medication and psychosocial treatment, community treatment
  - All 4 treatment groups showed benefit from baseline, with two medication treatment groups showing most benefit
  - Behavioural treatment not more effective than community treatment
- Behaviour therapy may be recommended as initial treatment if symptoms mild with minimal impairment, parental preference
- Behaviour therapy 10-20 sessions of 1-2 hours

Recommendation 7. The initial pharmacological treatment should be with an agent approved by the FDA

- Dexamphetamine
  - Short acting. Adderal, Dexedrine, Dextrostat
  - Long acting. Dexedrine spansule, Adderal XR, Lisdexamphetamine
- Methylphenidate
  - Short acting. Focalin, Methylin, Ritalin
  - Intermediate acting. Metadate ER, Methylin ER, Metadate CD, Ritalin SR, Ritalin LA
  - Long acting. Concerta, Daytrana patch, Focalin XR
- Atomoxetine
  - Strattera

Recommendation 7. The initial pharmacological treatment should be with an agent approved by the FDA.

- MAXIMUM DOSES >50kg
  - Dexamphetamine 60mg/day
  - Ritalin SA 100mg/day
  - Ritalin LA 100mg/day
  - Concerta 108mg/day
  - Strattera lesser of 1.8mg/kg or 100mg/day

Selection of agent

- Stimulants as first line particularly when no comorbidity present
- Meta-analysis of atomoxetine vs stimulant (Faraone et al 2003)
  - Effect size atomoxetine 0.62
  - Effect size MPH short acting 0.91
  - Effect size MPH long acting 0.95
- Atomoxetine preferred if
  - Active substance abuse problem
  - Comorbid anxiety
  - Tics
  - Severe side effects to stimulants such as mood lability or tics
  - ?Comorbid ASD symptoms

Medication targets

	INATTENTION	ANGER	ANXIETY	MOOD	TICS
STIMULANTS	++++	++	-	+	-
CLONIDINE	+	++	+	++	+++
SSRI's	+	+	+++	++	+
STRATTERA	+++	+++	++	+++	++
ANTIPSYCHOTICS	-	++++	+++	++	++++
MOOD STABILISERS	-	++	+	+++	+

Recommendation 8. If none of the above agents result in satisfactory treatment of the patient with ADHD the clinician should undertake a review of the diagnosis, and consider behaviour therapy and or other medication.

- Is poor response due to inaccurate diagnosis or undetected comorbid conditions such as affective disorders, anxiety disorders or subtle developmental disorders.
- Behaviour therapy and/or child psych referral
- Tricyclic antidepressants
  - Max lesser of 4mg/kg or 200mg
  - ECG baseline and after each dose increase
- Alpha adrenergic agonists
  - Max >45kg 400microgram/day
- Much lower effect sizes

Recommendation 9. During drug treatment for ADHD the patient should be monitored for treatment emergent side effects

- Stimulants
  - Decreased appetite, weight loss, insomnia, headache, emotional lability,
  - Bierderman 2002 no increase in tics c/f placebo
  - Wolraich 2001. ADHD and tic disorders show decline in tics when treated with stimulants, even after 1 year
  - If patient develops tics then alternative stimulant or atomoxetine should be tried
  - Alternative is to continue stimulant and add clonidine
- Atomoxetine
  - GI distress, sedation, decreased appetite, headaches
  - ?suicidal ideation: 12 controlled trials - 1357 ATX vs 851 placebo
    - 4/1000 in ATX, one attempt suicide no completion, none in placebo.

Cardiovascular issues

- FDA review 2006
  - 20 deaths DEX, 14 deaths MPH
  - Rate of sudden death children 1.3-8.5/100,000 pt years
  - Rate of sudden death in children with CHD 6% by age 20
  - MPH rate sudden death 0.2/100,000 pt years
  - DEX rate sudden death 0.3/100,000 pt years
  - ATX rate sudden death 0.5/100,000 pt years
- The rate of sudden death of children taking ADHD medications does not exceed the base rate of sudden death in the general population
- Cardiac consult if stimulants to be used in children with pre-existing cardiovascular disease

Recommendation 10. If a patient with ADHD has a robust response to medication and subsequently shows normal functioning then drug treatment alone is satisfactory

- MTA and M+MPT studies do not show an additive effect of psychosocial interventions in children without significant comorbidities
- Combined treatment did not yield superior outcome to medication only

Recommendation 11. If a patient with ADHD has a less than optimal response to medication, has a comorbid disorder, or experiences stressors in family life then psychosocial treatment with medication is often beneficial.

- MTA study shows strong evidence that patients with ADHD and comorbid disorders and or psychosocial stressors benefit from adjunctive psychosocial intervention
- Comorbid anxiety in particular predicted a better response to behavioural treatment particularly when the ADHD patient had both an anxiety and a disruptive behaviour disorder.

Recommendation 12. Patients should be assessed periodically to determine whether there is continued need for treatment or if symptoms have remitted. Treatment should continue for as long as symptoms remain present and cause impairment

- Follow up "several times" per year
- Review behavioural, academic and social functioning
- Height, weight, BP, HR
- Assess for emergence of comorbid disorders
- Given high level of maladaptive behaviours among adolescents medication treatment should continue and is likely to be highly beneficial
- If patient symptom free over at least 1 year then trial off medication may be indicated

Recommendation 13. Patients treated with medication should have their height and weight monitored throughout treatment

- Stimulant treatment may be associated with reduction in expected height gain, in first 1-3 years of treatment
- MTA study: decreased growth rates in stimulant vs non-drug treatment groups after 2 years, persisting for 3 years
- PATS study: After 12 months height (-1.38cm) weight (-1.3kg)
- Spencer et al: no height deficits c/f controls in childhood, a small reduction in height at puberty, but no difference in height in adulthood
- Faraone 2005. Stimulant induced growth delays are greater in first year of treatment but attenuate after that.
- Dose related. Significant effects only with MPH > 2.5mg/kd/day
- If crossing 2 percentile lines then drug holiday, reduced dose or alternative therapy indicated
- No evidence of reduction in final adult height

AACAP MEDIA PRESS RELEASE

- CHADD and AACAP Applaud Michael Phelps for Addressing Stigma of ADHD

  WASHINGTON, D.C., August 22, 2008 – Children and Adults with Attention-Deficit Hyperactivity Disorder (CHADD) and the American Academy of Child and Adolescent Psychiatry (AACAP) applaud Olympic gold-medalist Michael Phelps and his mother, Mrs. Deborah Phelps for educating the public about succeeding with attention-deficit/hyperactivity disorder (AD/HD).