The Complex ADHD child/adolescent

Rick Jarman

Case based discussion
Review of evidence for treatment
New Zealand
July 2010

Disclosures

- Presented at professional meetings sponsored by pharmaceutical companies
  - Eli Lilly
  - Janssen Cilag
  - Novartis
  - Merck Sharp and Dohme

AACAP 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

Pliszka S et al: J Am Acad Child Adolesc Psychiatry 2007;46:894-921

Complex ADHD

- Comorbid Oppositional Defiant Disorder
- Comorbid Learning Difficulties
- Comorbid Anxiety Disorders
- Comorbid Autism Spectrum Disorders
- Comorbid Substance Abuse
- Comorbid Tourette Disorder
- Comorbid family/psychosocial problems

Alex 17-7-92 (1)

- First referred Jan 1996, age 3 yrs 5 months
- Uneventful pregnancy, NVD. Advanced early development. Very active and alert infant. Very determined and intense toddler. Easily frustrated.
- "Bright boy, excellent language skills. Anger outbursts at home and child care. Yells and screams, hits others. Oppositional and defiant. Very active. Difficulty settling to task. Affectionate and cuddly. Good sense of humour. Liked by others".
- Behaviour management work with parents and child care. Routines, praise, rewards, ignoring, consequences.

Alex 17-7-92 (2)

- Next seen age 5 yrs 5 months. Carey Donvale preschool
- Diffficulty accepting change, complying with requests, handling frustration and anger. Unpredictable. Angry outbursts with sharing, turn taking, accepting direction. Hits out, kicks, spits, scratches children and staff
- Difficulty waiting turn, reluctance to share. Feelings of frustration and anger when he feels he is missing out. Refusal to comply with adult directions.
- Very active. Difficulty settling to task. Wanders off. Cant stand waiting. Highly strung

Alex 17-7-92 (3)

- Eldest of three children.
- Both parents full time professionals. Kids in child care 30 hours per week after full time nanny resigned because of Alex. Father distant, rigid, pedantic. Not affectionate. Mother frustrated, angered by inconvenience. Not much joy. Other kids in family different.
- Started school 1998. Bright. Difficulty staying in seat. Disruptive. Anger outbursts persist but settling.
- Trialled on Ritalin IR 10mg term 2, up to 1 tab TDS. Definite benefit.
- Further behaviour management work

Alex 17-7-92 (4)

- Progressively settled through early primary school. Bright, extended learning group. Very few friends, girls only. No party invites. Lacks animation. Doing well academically
- 2001 age 8, started sailing with father. Ritalin IR 10mg TDS continues. CBT anger management course
- Changed to Ritalin LA 30 age 11, then Concerta 36mg age 12 because of need for 12 hour coverage.
- 2005 very difficult transition to secondary school. Anger outburts, one involving a stick and a knife at school. Not coping with increased organisational and homework demands. More withdrawn.

Alex 17-7-92 (5)

- Updated neuropsychological testing
  - WISC 111 FSIQ 92% VIQ 98% PIQ 86%
  - "Mismatch between cognitive, affective and social development common in children with high intellectual ability. Behavioural and emotional characteristics of uneven development can include intensity and self criticism"
- Under-achieving relative to ability. Extra organisational help
- Trials off stimulants indicate they are still necessary for classroom functioning
- S/B child psychiatrist age 13. Aspergers/ADHD

Alex 17-7-92 (6)

- Anger outbursts resurfacing. Further behaviour management strategies discussed. Psychiatric counselling continues.
- Strattera 40mg/d increasing to 60mg/d trialled Nov 2006, age 14, with improvement from day 4.
- Much more settled, outgoing, relaxed, less intense. Anger controlled. Attention satisfactory. Mother feels improvements are significant, best he's ever been.
- Has remained on Strattera 60mg/d through year 11 2009. and year 12 2010. Excelling

Alex (7) - Summary

- Bright, intense, active, angry from early life
- Early emotional attachment problems
- Busy professional parents. Not much nurturing or affection. Father distant (?Aspergers). Long hours in child care
- Capable academically but underachieving
- ADHD and later Aspergers diagnoses
- Response to stimulants
- Various psychological therapies
- Better on Strattera. Why?

Medication targets

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

Adrian 21-8-92 (1)

- First seen 2004 age 11 for additional opinion re previous diagnosis ADHD.
- Hyperactive, impulsive, distractible, and aggressive from early life
- Only child, professional parents, F suspected as having ADHD. Parents divorced, remarried, half sibs and step sister.
- On compounded dexamphetamine 10mg 3 caps mane, dexamphetamine SA 5mg 1 tab late afternoon (35mg/day). Problems at end of afternoon
- Wildy hyperactive off meds. "Doesn't know he has ADHD"
- Third primary school
- "High IQ". Academically capable but underachieving. Social problems

- CBCL, TRF, ADHDRS.

- **Severe ADHD, comorbid ODD/anxiety, No LD, Very high requirement for stimulants**

Adrian 21-8-92 (2)

- Tried Concerta 36 increasing to 72mg/d. Not sure
- Back to Dexamphetamine SA 35mg/d given tds
- Classroom behaviour management work
- Parent training
- Individual counselling including social skills work

- Remains relentless, demanding, obsessional, poor self reflection skills

- Dexamphetamine short acting increased to 40mg/d given tds

- Moved to Preshill year 7. Unsettled, disruptive, argumentative
- Psychological counselling

- "Now knows he has ADHD"

- Swapped to Ritalin 10 up to 70mg/d. Perhaps a little better
- Added Fluoxetine 20mg/d. More hyped, stopped
- Parents flustered angry, no joy in parenting

Adrian 21-8-92 (3)

- Age 14, child psychiatry opinion. Severe ADHD, not BP
- Psychology testing high average IQ
- Counselling continues
- Audiology testing STAM weaknesses, figure ground discrim problems
- Speech pathology testing CELF average receptive/expressive lang

- Age 15 Ritalin stopped, Strattera trialled up to 80mg/d
- Depressed, suicidal ideation, too hyped at school
- Strattera stopped Ritalin SA recommenced 80mg/d, then Concerta 72mg/d
- Epilim added 500mg BD

- Age 16 moved to boarding school in country Vic Monivae College
- Best report ever
- Seeing school counsellor

Adrian 21-8-92 (4)

- Age 16 palpitations, dizzy spells, anxiety
- Cardiology referral ECG, bloods all nad
- P 90/min reg, BP 110/60

- Concerta reduced to 36mg/d
- Epilim continues 1400 mg/day

- Stable over recent months
- No further dizzy spells
- Concentration adequate
- Mood steady

- ?ADHD vs Bipolar 11

Medication targets

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

Wayne 5-11-86 (1)

- From Hamilton, country Victoria
- First seen age 10 in 1996
- Previous diagnosis ADHD on Ritalin IR 20mg bd
- Associated mild learning difficulties. Average IQ
- Single mum, one younger sister (hearing impaired and with learning difficulties). Stable family situation. Homework a battle
- Clear difference on and off meds at school by parent report.
- Requested to trial dexamphetamine age 14 as comparison, reported better

Wayne 5-11-86 (2)

- Left school age 16, two labouring jobs, sacked
- Cant function without dexamphetamine, now increased to 30mg/d
- TAFE age 17 certificate 2 info tech & multimedia studies, dropped out
- Age 18 nightclub work on weekends, bartending, DJing. Other part time work pressing wool
- "Happy making money"

- Sister then age 14 also brought to see me by mother wants to try dex because of learning difficulties. CBCL/TRF/ADHDQ indicated learning delays, attentional problems (mild). Ongoing need for meds even after she left school in 2007 to do horticulture course

Wayne 5-11-86 (3)

- Wayne, age 19, working as baker in Bordertown. Living on own, frustrated depressed. Calls home occasionally. Still needs dexamphetamine, taking up to 40mg/d. Advised to keep doses modest to 20mg/d if possible
- Age 22, no work for last year or two, moved back to Hamilton to live with mother. Dexamphetamine 20mg/day

- Mother called for repeat script on 25/9/2009, says repeats lost
- Called Medicare Australia for authorisation, refused
  - Last script written 23/6/09 200 tabs with 3 repeats
  - Filled original 200 tabs 30/6/09
  - Filled first repeat 200 tabs 21/7/09
  - Filled second repeat 200 tabs 11/8/09
  - Filled third repeat 200 tabs 1/9/09

- Average 10 tabs (50mg) per day over 3 months on script for 4 tabs per day (20mg)

Wayne 5-11-86 (4)

- Overuse of stimulant meds – redirection/abuse
- For how long?
- What about sister's meds?

- Continuing to supply meds to young adult when no external verifiable source to confirm value. Self report an issue in adult diagnosis

ADHD comorbidities

	Prev	Odds Ratio
Oppositional Defiant Disorder	54-84%	10.7
Conduct Disorder	25%	
Substance Abuse Disorders	10%	7.9
Learning and Language disorders	25-35%	
Anxiety Disorders	30%	3.0
Pervasive Developmental Disorders	0-15%	
Depressive Disorders	0-33%	5.5
Bipolar II	15%	
Tourette's Disorder	5-10%	
Developmental Coordination Disorder	10%	
Antisocial personality disorder (adulthood)		2.5

Angold A et al: J Child Psychol Psychiat 1999;40:57-87
Loeber et al: J Am Acad Child Adolesc Psychiatry 2000;39:1468-1484130
Semrud-Clikeman M et al: J Am Acad Child Adolesc Psychiatry 1992:31:439-448
Piek JP et al. Devel Med Child Neurol 1999;41:159-165
Freeman et al: European Child Adolesc Psychiat 2007;16(suppl)9:I/15-I/23

ADHD with comorbid anxiety

- Stimulants alone
- Stimulants + SSRI
- SSRI alone
- Other antidepressants alone
- Atomoxetine

ADHD and comorbid anxiety

- Two randomised controlled trials
  - Diamond et al 1999. Four month trial of MPH. The presence of anxiety did not influence the response to the medication or the numbers of adverse events
  - Geller et al 2007. Twelve week trial of ATX in the treatment of ADHD and comorbid anxiety. Reduction in symptoms of both ADHD and anxiety, but ATX associated with significantly more reports of decreased appetite and weight loss c/f placebo
- NHMRC Australia 2008
  - Psychosocial management considered in ADHD and anxiety
  - Consider MPH or ATX to treat ADHD symptoms
  - If anxiety symptoms do not respond consider SSRI either alone or in combination with a medication to treat ADHD

Diamond I et al. J Am Acad Child Adolesc Psychiatry 1999:38:402-409
Geller D et al: J Am Acad Child Adolesc Psychiatry 2007:46:1119-1127

ADHD and comorbid PDD

- Stimulant alone
- SSRI alone
- Atomoxetine
- Risperidone alone
- Stimulant + SSRI
- Stimulant + Risperidone
- Risperidone + Mood stabiliser

ADHD and comorbid PDD

- Three RCT demonstrate benefit of MPH over placebo in reducing hyperactivity, inattention and impulsivity in children with ASD
  - RUPP Autism Network study: 49% MPH response 8% placebo response
- One study demonstrated benefit of ATX over placebo in reducing hyperactivity and impulsivity in children with ASD
- NHMRC Australia 2008
  - In children with an ASD use of stimulant or ATX should be considered to treat ADHD symptoms
  - Careful monitoring is required due to the risk of exacerbating ritualistic and agitated behaviours.

Handen BL et al. J Autism Dev Disorders 2000;30:245-255
Posey DJ et al. Biological Psychiatry 2007;61:538-544
Research Units on Pediatric Psychopharmacology. Arch Gen Psychiatry 2005:62:1266-1274

ADHD and comorbid depression

- Bangs et al 2007. Nine week RCT ATX vs placebo in treatment of ADHD and comorbid MDD. Significant improvement in ADHD symptoms but not depressive symptoms in ATX group

- NHMRC Australia 2008
  - Consultation with psychiatrist considered
  - Non-pharmacological management considered
  - Are stimulants aggravating depression?
  - Are illicit drugs aggravating depression?
  - Consider ATX in ADHD and depression
  - Consider stimulants in ADHD and depression
  - Consider SSRI's in adolescents and adults with ADHD and depression

Bangs ME et al. J Child Adolesc Psychopharmacol 2007;17:407-420

Lifetime prevalence of DSM disorders in adults

Kessler RC et al: Arch Gen Psychiatry 2005;62:593-602

Nationally representative sample 9282 subjects over 18 years
Face to face household interview using WHO Mental Health Survey

Lifetime	
Anxiety Disorders	28.8%
Mood Disorders	20.8%
Impulse Control Disorders	24.8%
Substance Use Disorders	14.6%
Any Disorder	46.4%

Substance Abuse

Any one of A <u>and</u> both B and C

A. Recurrent failure to meet important responsibilities due to use
   Recurrent use in situations when this is likely to be physically dangerous
   Recurrent legal problems arising from use
   Continued use despite recurrent problems aggravated by the substance use
B. These symptoms have occurred within a 12 month period
C. Doesn't meet criteria for dependence

Substance Dependence

Any three of A and B

A. Tolerance. Needing more to become intoxicated or discovering less effect with same amount
   Withdrawal.
   Using more or for longer periods than intended
   Desire to or unsuccessful efforts to cut down
   Considerable time spent in obtaining the substance or using or recovering from its effects
   Social, work or recreational activities given up because of use
   Continued use despite knowledge of problems caused by or aggravated by use

B. Problems present during at least 12 months

Detecting substance use and abuse

Winters KC, Kaminer Y. Screening and assessing adolescent substance use disorders in clinical populations. J Am Acad Child Adolesc Psychiat 2008;47:740-744

- Direct questioning
- Paediatricians not good at detection
- Urine tests
- Validated self report measures
  - Achenbach YSR
  - CRAFTT screener
  - Personal Experience Screening Questionnaire (PESQ)
  - Teen Addiction Severity Index (T-ASI)
  - Personal Experience Inventory (PEI)

Key questions

- Does stimulant drug use increase the risk for substance abuse later in life?
- Do ADHD medications have the potential for abuse?
- What is the distinction between drug abuse and misuse/diversion with respect to ADHD medication

Theoretical concerns

- Stimulants such as DEX and MPH chemically similar to cocaine
- Potential for stimulants to lead to increased sensitisation to later stimulant exposure.
- Studies in mammals suggest repeated stimulant exposure leads to subsequently greater craving and self administration of stimulants
- No evidence that this happens with the therapeutic doses of medical stimulants used in humans

Is ADHD a risk factor for SUD?

Biederman J et al. J Am Acad Child Adolesc Psychiat 1997;36:21

- 140 ADHD, 120 controls baseline and 4 years later
- Baseline mean age 11.5. Follow up mean age 15.2
- Cases and controls both had 15% rate SUD
- Increased risk with comorbid CD (45%)
- Marijuana by far commonest drug abused

ADHD children grown up

Barkley R et al. J Child Psychol Psychiat 2004;45:195-211

- 13 year follow up 147 ADHD and 73 controls
- Higher rates than controls of
  - Antisocial acts
  - Arrests
  - Property theft
  - Disorderly conduct
  - Assaults
  - Carrying a concealed weapon
  - Motor vehicle accidents, speeding fines
  - Illegal drug possession
  - Substance use and abuse
- Comorbid CD explains almost all the variance in this increased risk

Shared comorbidity between ADHD and SUD in adults. Problem issues

- 15% of adults with ADHD have SUD
- 20% of adults with SUD have ADHD
- Difficulty with DSM IV diagnosis of ADHD in adults, given that criteria developed for primary age children.
- Symptoms of intoxication and withdrawal may mimic ADHD symptoms
- Adult patients may feign ADHD symptoms to obtain stimulant meds

Levin FR, Upadhyaya HP: Diagnosing ADHD in adults with substance use disorder. Journal of Clinical Psychiatry 2007;68:18-30

Does stimulant treatment lead to substance use disorders

Faraone S, Wilens T. J Clin Psychiat 2003;64 suppl:9-13

- Meta-analysis 7 studies
- Exposure to stimulant therapy for ADHD does not increase the risk for developing substance use disorders, but is in fact protective against it.
- Stimulant medication treatment of ADHD reduces the risk of SUD by 50% to levels well within the normal population risk

Another meta-analysis

Wilens T et al. J Child Adolesc Psychopharm 2005;15:787

- Four adolescent and five adult studies in ADHD with comorbid SUD (n=222)
- Treating ADHD pharmacologically in individuals with ADHD and SUD has a moderate impact on ADHD <u>and</u> SUD symptoms

Adolescent prescription misusers

Schepis T et al. J Am Acad Child Adolesc Psychiat 2008;47:745

- 2005 National Survey of Drug Use and Health
- 18,678 adolescents 12-17

- 8.2% misused a medication
- 3.0% endorsed symptoms of SUD
- Predictors of misuse
  - Poor academic performance (OR 2.9)
  - Past year major depression (OR 3.1)
  - Higher risk taking levels (OR 3.6)
  - Past year of alcohol (OR 7.3), cigarettes (OR8.6), marijuana (OR9.9), cocaine (OR10.7)

Misuse and diversion of stimulants prescribed for ADHD

Wilens T et al. J Am Acad Child Adolesc Psychiat 2008;47:21-31

- Literature review 21 studies, 113,104 subjects
- Rates of past year non-prescribed stimulant use
  - Late primary/Secondary school 5-9%
  - College age 5-35%
- Lifetime rates of diversion 16-29%
- Risk factors
  - Caucasian, members of fraternities/sororities, lower academic achievement, IR rather than extended release preparations

Sources of prescription misuse

Schepis T, Krishnan-Sarin S. J Am Acad Child Adolesc Psychiat 2009;48:828-836

- Rise in prescription misuse last 10 years
- Decline in use of other illicit drugs, alcohol or tobacco (except ecstasy)
- 2005 National Survey of Drug Use and Health
  - 36,992 between 12-17 years
  - Lifetime prevalence of misuse
    - Opiods 10.1%
    - Tranquillisers 3.0%
    - Stimulants 3.4%

Sources of prescription misuse

1. Friends or relatives for free 41%
2. Purchasing 21%
3. Physician 22%
4. Theft 10%
    1. From medical source 0.8%
    2. Stolen forged prescription 0.5%

Australian data limited

- Queensland Crime and Misconduct Commission
  - “Illicit diversion and abuse of ADHD meds only a minor problem”
- Aust School Students Alcohol and Drug Survey
  - 8% of students had (ever) used Dex or Ritalin without doctors prescription
  - Access by being given them, bought them, or traded something for them

Drug & Alcohol Office. Government of West Australia. Statistical Bulletin No 37. Summary of WA results Australian School Students Alcohol and Drug Survey 2005, 2007

NHMRC 2008

- The use of stimulant medication to treat people with ADHD does <u>not</u> increase the risk of developing substance use disorder
- Medication treatment for ADHD with substance misuse should only be provided by a medical practitioner with expertise in both conditions
- ATX should be the first medication trialled if the person with ADHD has a comorbid substance use disorder

National Health & Medical Research Council Australia. Guidelines on Attention Deficit Hyperactivity Disorder (ADHD). Draft for Public Consultation 2008. www.NHMRC.org

Treatment resources for substance abuse

- Victoria
  - Direct line 1800-888-236
  - Internet www.health.vic.gov.au/drugs
- Australian Drug Information Network (ADIN)
  - Internet www.adin.com.au

Summary

- Patients with ADHD and SUD have an earlier age of onset of SUD, and may take longer to achieve remission than those with SUD alone. They are likely to have a longer course, poorer outcome, and higher rates of psychiatric comorbidities.
- Stimulant meds may be misused and diverted
- Stimulant meds do not exacerbate SUD and may help it.
- Extended release stimulant meds and non-stimulants may be less likely to be misused or diverted than short acting stimulants
- Treatment of SUD is more difficult if ADHD symptoms are not controlled. Weigh up risks individually
- Use standardised tools for assessing drug use, and think about toxicology screens
- Be familiar with local resources for helping SUD youth