

ADHD Drugs

Mixing and Matching

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As much as one might wish that a “pure” diagnosis would be followed by a single curative action, this is rarely the case with attention deficit hyperactivity disorder (ADHD). In practice, drugs have been used more frequently and in increasing combination to achieve maximal therapeutic benefit, in an attempt to reduce or eliminate problem behaviours. Unfortunately much of this experience is not evidence-based, particularly where combination medications are used.

What are the parameters of ADHD?

The classical symptoms are inattention, hyperactivity, and impulsivity. Additional anxiety and depression can occur, perhaps because of negative feedback from caretakers. Specific learning disorders are also often present (60%). Caretakers who try many different methods to help the child, may feel frustration, anger, and guilt. The condition itself lacks definition in the early years when the child is free to range, but becomes evident when the restrictions of school and society are applied. ADHD must be present by the age of seven in more than one location.

Darren's history

Darren, 15, lives with his mother, stepfather, and three half-siblings.

Darren's IQ is average. At five, he was diagnosed with attention-deficit

hyperactivity disorder and Tourette's disorder. He was treated with clonidine 0.05 mg orally four times a day replacing Ritalin®.

Due to clumsiness, and staring spells, Darren was referred to a neurologist when he was nine. An electroencephalogram was consistent with Rolandic epilepsy (no spike and wave). He was started on carbamazepine after one seizure.

Darren sexually abused his half-siblings after being victimized at school. He underwent psychotherapy. During his teen years, he showed anger and aggression. Haloperidol drops replaced the clonidine he was taking. His hyperactivity was controlled with d-amphetamine. Pimozide replaced haloperidol, and increasing pimozide created extrapyramidal symptoms.

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Can ADHD be treated with drugs alone?

The situation-specific plan may include medication or social manipulation, teaching, aids to attention and memory, and increased supervision. This article deals with medications only, and there is good evidence these can be used alone to control most of the symptoms that create problems. However, treatment resistance, concomitant problems, and side-effects may require further drugs (Figure 1).

What are the molecular manipulations of amphetamines?

The tricyclic antidepressants, methylphenidates, and more recently, bupropion, have been the mainstay of treatment for ADHD for 50 years. Early in the history of treatment, chlorpromazine was also identified as useful, especially with the more impulsive and hyperactive children. These two types—stimulant and antipsychotic—have continued to provide the primary treatment options for ADHD. The antipsychotics seem to work better at the impulsive/hyperactive end of the spectrum of ADHD, and the stimulants at the inattentive end. Anxiety and movement disorders are additional problems. They demand different medications and carry the same potential difficulties as in adult practice. Over-treatment with any medication can produce iatrogenic effects that may need dose adjustment or the addition of another substance.

What are some drug-induced problems and treatments?

Stimulants can produce a variety of symptoms and signs as side-effects, including direct results and the revealing of otherwise hidden problems. The group includes insomnia,

Darren's results

Diagnosis

- ADHD-hyperactive/impulsive type
- Tourette's disorder

Medication

- Pimozide 2 mg three times a day
- Dexedrine® 25 mg as spansules am
- Carbamazepine 800 mg three times a day

anorexia, depression, paranoid ideation and growth delay. Tics, obsessive compulsive disorder and mood episodes occur due to this problem. Depression, hypomania, and severe cyclical conduct problems may suggest the need for other diagnoses and treatment (Figure 2).

What are the drugs for comorbid conditions?

Comorbid conditions include learning, speech, and language disorders with frustration and anger usually reserved for home. Conditions also include anxiety disorder in its various forms and other developmental problems:

- enuresis,
- encopresis,
- conduct disorder,
- Tourette's disorder,
- alcohol related neurologic disorders,
- thyroid disorders; and
- mood disorders.

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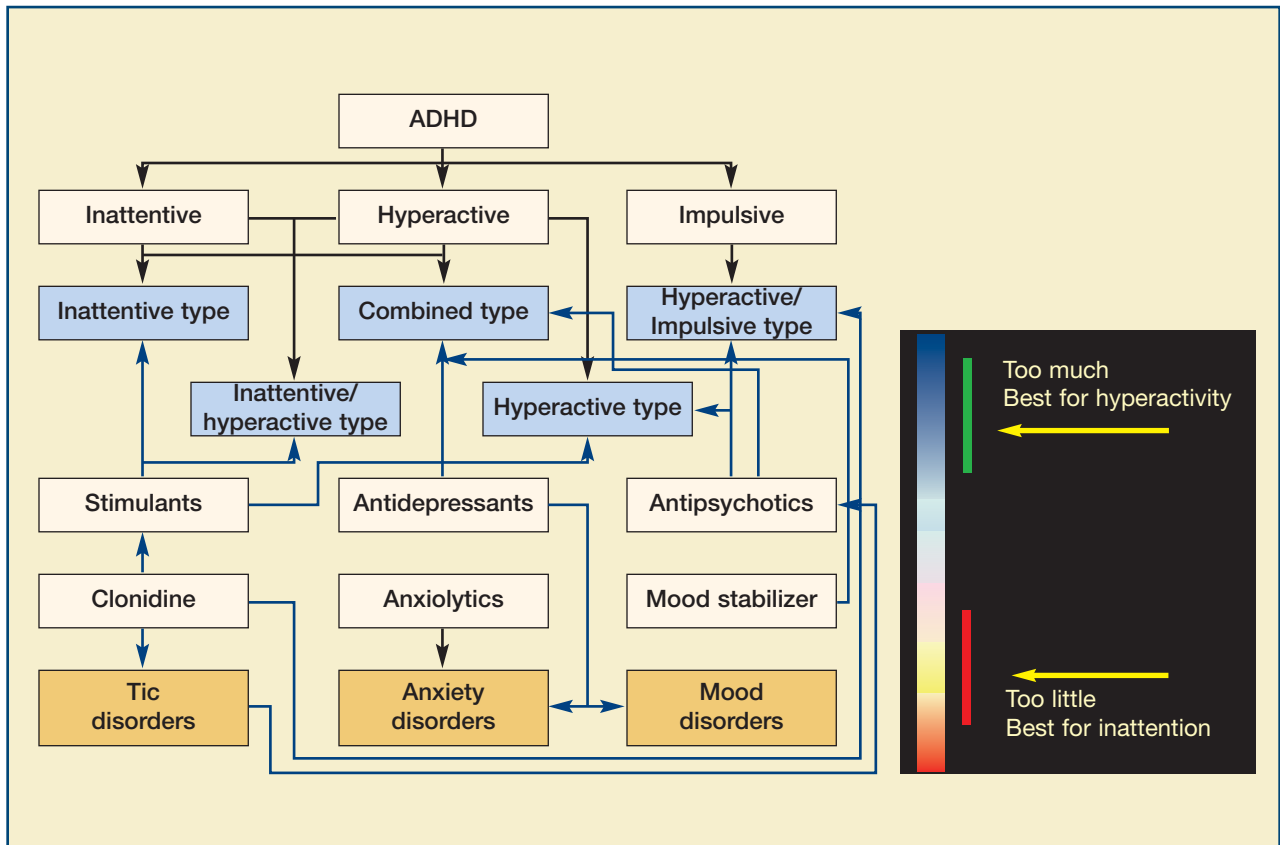


Figure 1. Varieties of medications for ADHD.

Concomitant medications for these conditions may be required with caution about interactions, direct effects and safety. Most medications carry an unknown quality of effects on future years, and therefore ethical pharmaceutical companies have been reluctant to approve research on the under-18 group. Child psychiatrists have been adventurous in pursuing the goal of symptom relief.

What are future options?

Perhaps the future will bring newer medications to help bridge gaps, smooth presentation, and lengthen the effect more permanently (weeks, months, years, or forever).

Delayed release, patches, and depot injections, which have been realized in other products, offer some promise.

Frequently Asked Questions on: ADHD Drugs

Questions:

Some medications are not recommended for patients under 18. Are they safe?

Is it true that a combination of methylphenidate and clonidine is dangerous?

Why are you reluctant to use risperidone?

How about comorbid anxiety and OCD with ADHD?

Answers:

Yes. The “not recommended” comment is because Health and Welfare (H&W) has not received good evidence these medications have been adequately tested on children. Research studies are not large enough. Due to this, H&W will not approve a medication for use in children. Physicians, however, are able to prescribe medication shown to be safe with adults to children, if they consider it appropriate.

Yes. There were some cases in which a combination of clonidine and Ritalin® (methylphenidate) appeared to cause cardiac events. On closer examination, it was found that subjects were already cardiac-compromised when given the medication. I have been using clonidine as a staple with methylphenidate, especially where tics develop, and I am reluctant to add risperidone.

Because of the ease with which children develop dystonias and dyskinesia. Also, because of the risk of obesity and Type 2 diabetes in both sexes, and raised prolactin levels in girls.

I would consider pediatric autoimmune neurologic disorders associated with Streptococci as a possibility, and look at the streptolysin titre to be followed by a more specific a-haemolytic streptococcus to determine its presence or change in titre. Antibiotics would be a first-choice treatment then.

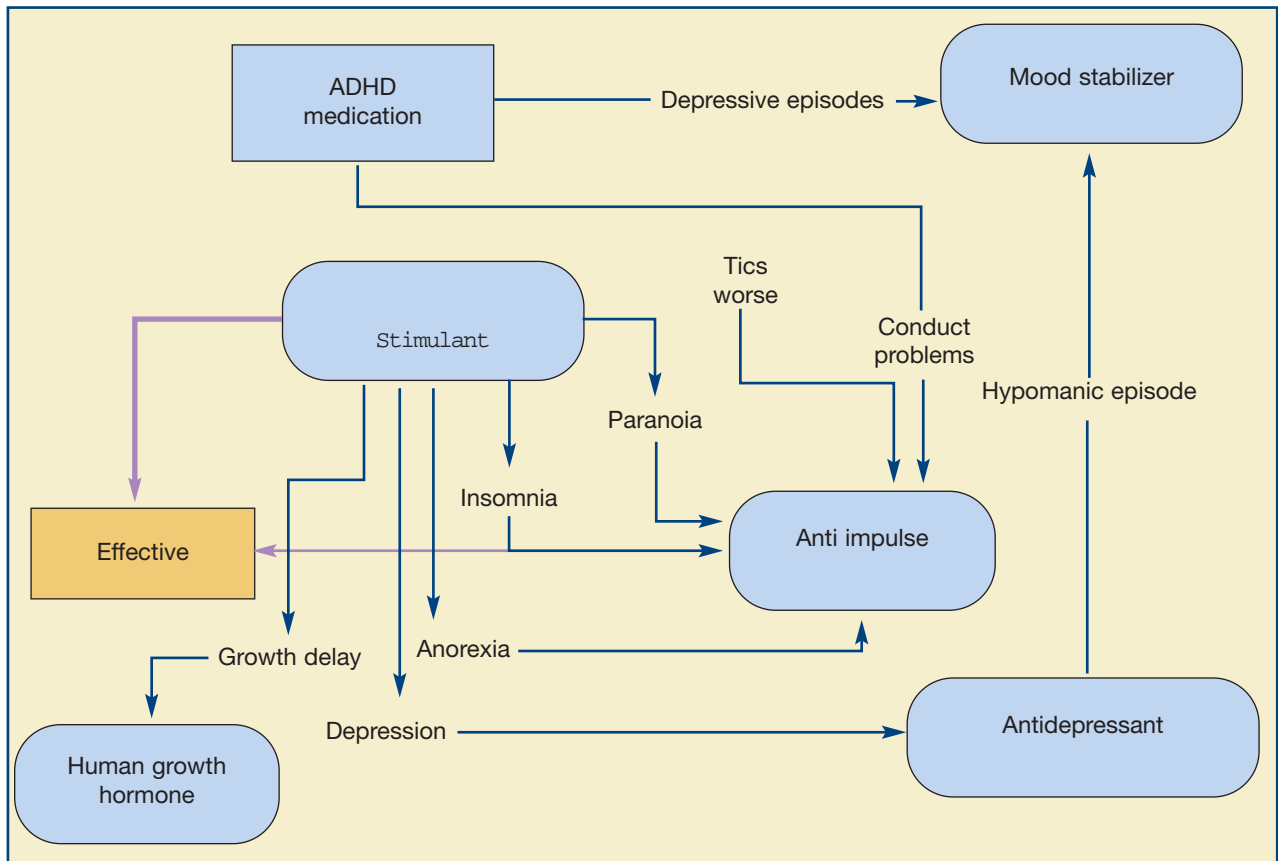


Figure 2. Medication choices and side-effects.

What are the new primary medications?

Canadian pharmaceutical companies are bringing a number of new products onto the market this year and in succeeding years to combat present problems. These include long-acting methylphenidate, long acting dexamphetamine salts mixture, and atomoxetine.

Better anti-iatrogenesis implies the avoidance of potentially problematic medications, the development of less side-effect prone medication, and looking for several effects at once. An example of the latter is the use of risperidone with methylphenidate. Appetite suppression is countered with appetite enhancement. Insomnia is set against somnolence. Impulsiveness control is supplemented with

inattention and hyperactivity control in the prepubertal group.

Some examples of safer combinations with supportive evidence are methylphenidate and clonidine/guanfacin; methylphenidate with risperidone; and lithium; and methylphenidate and sodium divalproex.

In conclusion...

Medications for ADHD have included those needed to control the primary symptoms and signs: inattention, hyperactivity and impulsivity. These have not changed much over the years, but more attention has been paid to trying to obtain fairly complete and steady coverage, to reduce the consequential side-effects and to deal with comorbid conditions. The comorbid

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conditions are usually developmental and involve learning, memory, and executive functions, but can also involve mood and movement disorders.

Physicians, patients, and parents choose medications on the basis of preference. They include some of the most powerful psychiatric drugs prorated for children. There has been little research on the combinations, although some have been tested successfully.⁸⁻¹¹ [CME](#)

Take-home message

- Polypharmacy in ADD is still on the rise.
- Combination therapy can be safe and effective but requires close attention to side-effects, inter-reactions and monitoring.
- Mood stabilizers and some antidepressants have joined stimulants and antipsychotics in management as well as anxiolytics.

Net Readings

1. Doctor's Guide:
www.docguide.com/
2. American Academy of Pediatrics:
www.aap.org/policy/ac0002.html

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