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Prescribing psychotropic medication
in children and adolescents

GPs require some knowledge of the pharmacological management of children and adolescents with psychiatric problems as they may be asked about treatment options or consulted about side effects; they may also undertake treatment of less complicated conditions.

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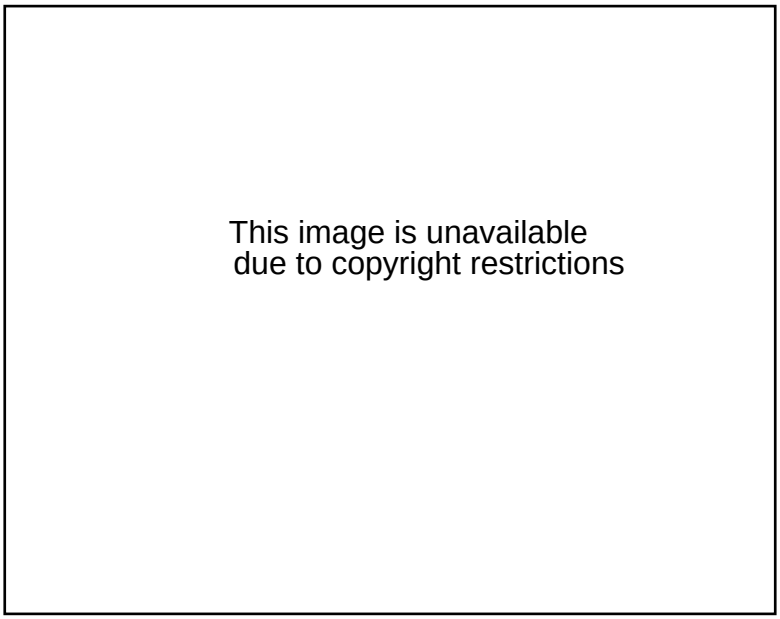
Common childhood psychiatric disorders that require pharmacological treatment are attention deficit hyperactivity disorder (ADHD) and anxiety. Less frequently encountered conditions that require treatment include obsessive compulsive disorder (OCD), depression, tic disorders, aggressive behaviour associated with autism and intellectual disability, juvenile onset bipolar affective disorder and psychosis. The pharmacological treatment of uncomplicated OCD, anxiety and tic disorders can be undertaken by GPs who fully understand the treatment options and side effects; however, other more complex or controversial disorders are better managed by specialist services.

Misgivings exist about drug treatment for emotional and behavioural problems in young people. A recurring theme is that we are trying to 'medicalise' problems that are social in origin. It would certainly be unethical to prescribe medication instead of attending to fundamental predicaments that can affect children and adolescents such as neglect, maltreatment or bullying. It is also reasonable to ask the question, 'Will the child or adolescent (distinct from carers or teachers)

IN SUMMARY

- **There are nonpharmacological options for most children and adolescents with psychiatric disorders or problems.**
- **Pharmacological treatment of uncomplicated obsessive compulsive disorder, anxiety and tic disorders can be undertaken by GPs who fully understand the treatment options and side effects; however, other more complex or controversial disorders are better managed by specialist services.**
- **When treating a child or adolescent for a psychiatric disorder, the doses recommended in this article should be followed; however, in patients who have a poor treatment response, doses in the upper range may be necessary.**
- **An adequate trial of the drug, in adjusting and scheduling of doses, should be given before considering a change in treatment.**
- **Growth parameters should be routinely monitored when following up patients who have been prescribed psychotropic medication.**
- **If treatment response is inadequate, adherence to therapy should be monitored before increasing the medication dose. If multiple medications seem necessary, a specialist review should be sought.**
- **In patients who are stopping therapy, it can be necessary, particularly with some medication, to taper the doses to avoid the development of a discontinuation syndrome.**

receive benefit from this treatment?' If the answer to this question is uncertain, changes in the child or adolescent's environment that may help to improve the situation should be considered first. Objections to psychotropic treatment can be associated with a reluctance to acknowledge that young people may experience severe emotional distress or a notion that to endure distress is character building. Some believe that to deny a person effective treatment to alleviate severe emotional distress is as undesirable as denying a person in physical pain effective analgesia. Good prescribing practice involves more than simply writing a script. It requires patient and carer education, regular monitoring of effectiveness and safety of the drug, and adjusting and scheduling of doses to optimise treatment benefit. It also requires patient support and advocacy. Finally, there should be a timetable for treatment discontinuation.



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ADHD

Children and adolescents with ADHD respond well to methylphenidate or dexamphetamine. Although these are safe and well researched medications, regulations in most States and Territories prevent GPs from initiating them; however, in some States GPs can continue treatment. Alternative medications that GPs can prescribe include atomoxetine (Strattera) and clonidine (Catapress). (Note, however, that ADHD is not a formally recognised indication for clonidine in Australia.)

Methylphenidate is available in Australia in a short-acting form (immediate release; Attenta, Ritalin 10) with about a four-hour duration of action, an intermediate-release form (Ritalin LA) and as a slow-release form with a 12-hour duration of action (Concerta Extended Release). With the PBS listing of Ritalin LA on 1 April 2008, all the above mentioned forms of methylphenidate and dexamphetamine will be available on the PBS (authority required).

Dexamphetamine is only available in Australia as a short-acting preparation with a duration of action of four to six hours. Short-acting preparations are typically taken two or three times per day, including a dose during the school day. Adherence is usually reliable during the primary school years when school staff may supervise administration of medication, but is often unreliable in the high school years. For this reason, longer-acting preparations are recommended for teenagers.

Typical side effects of methylphenidate and dexamphetamine include appetite suppression (leading to weight loss), increased sleep latency and rebound activation as the medication effect wears off. Weight loss can be minimised by encouraging the patient to eat a solid breakfast before the first dose of stimulant is taken and snacking in the evening following the offset of action of the drug. Sleep problems are common in children with ADHD who are not receiving medication. For patients vulnerable to insomnia, doses of immediate-release medication in the late afternoon or evening should be avoided, and intermediate rather than long-acting methylphenidate should be used. Rebound is less of a problem with the longer-acting compounds. Another strategy for avoiding rebound is to use a reducing schedule dose of immediate-release medication, for example, one and a half tablets with breakfast, one tablet with lunch and half a tablet after school.

Atomoxetine is a selective noradrenergic reuptake inhibitor that was first approved for the treatment of ADHD in Australia in 2004. Unlike stimulant medications, atomoxetine has to be administered for several weeks before a treatment effect is achieved. With a single daily dose, the drug will usually provide 24-hour coverage of symptoms. Atomoxetine is listed on the PBS

(authority required) when initiated by a paediatrician or psychiatrist for use in patients aged 6 to 18 years in whom:

- treatment with dexamphetamine or methylphenidate poses an unacceptable risk due to a history of substance abuse or misuse (other than alcohol) and/or the patient has a comorbid tic disorder, Tourette's syndrome or severe anxiety disorder
- treatment with dexamphetamine or methylphenidate has resulted in the development or worsening of a comorbid mood disorder of a severity necessitating permanent stimulant treatment withdrawal
- treatment with dexamphetamine or methylphenidate has caused intolerable side effects.

GP initiations and prescribing of atomoxetine outside the PBS parameters are not reimbursed (see the full Schedule). Most of the evidence for the efficacy of atomoxetine has been obtained in patient populations with uncomplicated ADHD. Atomoxetine is commenced at a dose of 0.5 mg/kg per day, titrating up in weekly steps to 1.2 to 1.4 mg/kg per day. Atomoxetine may be moderately sedating during the first few weeks of treatment. For this reason, I recommend commencing treatment with an evening dose and then switching to a morning dose once tolerance to the sedative effect has developed. Decreased appetite and dyspepsia are common during the first few weeks of treatment, but usually less marked than that seen with stimulant medications.

The alpha-agonist clonidine is typically used in combination with stimulant medication. It is helpful in reducing comorbid aggression, although an additional benefit can be to counter insomnia. Clonidine is initiated at a dose of 25 to 50 μg twice or three times daily, then titrated up according to effect and sedation. Carers must be educated in the use and the safe storage of clonidine as even small overdoses may be harmful. In addition, sudden cessation of the drug can be hazardous as it will cause a rebound rise in blood pressure. I have encountered this problem a few times when patients have had to undergo emergency surgery.

Anxiety, obsessive compulsive disorder or depression

Children and adolescents with anxiety disorders respond well to psychological treatments. Indications for medication include significant impairment, such as school refusal, a poor response to psychological treatment and severe episodes of anxiety such as panic disorder.

OCD may also affect children and adolescents, and in its more severe form is disabling. The content of the obsessions, particularly if they are of a sexual nature, can be distressing and may lead to secondary depression. OCD symptoms can be present in a range of other psychiatric conditions, but the principles of treatment are the same. Depression in children and adolescents can be overlooked as it often has an insidious onset and is characterised by irritability rather than low mood.

Children and/or adolescents with anxiety, OCD or depression usually respond well to serotonin reuptake inhibiting drugs (SSRIs), although ironically the least impressive results are seen in children with depression. Patients with these disorders also respond well to structured psychotherapies such as cognitive behaviour therapy. There is no great advantage in combining pharmacotherapy with psychotherapy. Pharmacological treatment is indicated if the problems are severe. For patients with anxiety, OCD or depression who are experiencing significant insomnia, fluvoxamine (Faverin, Luvox, Movox, Voxam) taken in the evening can be helpful, as it tends to be sedating. In most other cases, fluoxetine is recommended as first-line medication, as its long half life overcomes the problems associated with missed doses.

Children are commenced on a quarter of a standard dose of a SSRI, which is then titrated according to tolerability at weekly intervals. Teenagers commence on half of the standard dose. Doses required to achieve benefit often approach or exceed typical doses given to adult patients. Persistence is needed as it may be many weeks before benefit is apparent. Doses that are titrated too rapidly can cause problems of activation and, rarely, the serotonin syndrome. This syndrome is characterised by neuromuscular symptoms such as spasms, autonomic symptoms such as sweating and shivering, and mental state changes such as confusion. Onset of these symptoms warrants hospitalisation.

Children and adolescents who participated in treatment trials for depression were twice as likely to experience suicidal thoughts or to self-harm if they received a SSRI than if they received placebo. Put in perspective, the absolute rates of suicidal thoughts and self-harm were low (4%) for the SSRI-treated group, and are similar to the community prevalence of these problems. Nevertheless, weekly contact with the patient to monitor risk during the early phase of treatment is recommended. Treatment should be continued for at least a year, then tapered gradually to avoid causing a withdrawal syndrome characterised by influenza-like symptoms and agitation.

Trials of benzodiazepines in children with anxiety have not demonstrated significant benefit over placebo and their use is discouraged. For cases of overwhelming distress arising from acute psychological trauma I sometimes prescribe a brief course of a sedating atypical antipsychotic such as quetiapine (Seroquel).

Aggressive behaviours associated with autism and intellectual disability

Aggressive behaviours associated with autism and intellectual disability arise from a combination of limited problem-solving skills and a low threshold to arousal. Such problems are distressing for the child's carers. Controlled trials have found risperidone (Risperdal) superior to placebo in treating such symptoms.

Risperidone is now listed on the PBS (authority required; streamlined) for patients aged less than 18 years with autism who manifest aggressive or injurious behaviour to self or others. For a PBS rebate, treatment must be under the supervision of a paediatrician or psychiatrist and must be provided in combination with nonpharmacological measures.

In my experience, although the initial impact of risperidone on behaviour can be dramatic, treatment benefit typically attenuates over the ensuing months. Warning carers of this possibility is an essential part of therapeutic care, as their expectations can be high. Risperidone is initiated at a dose of 0.25 or 0.5 mg per day, titrated according to response and tolerability. Because of the sedative action, I recommend starting with an evening dose but switching to a morning dose if there is an inadequate treatment effect. Twice-daily dosing can be helpful to ensure symptom coverage throughout the day. As with many of the atypical antipsychotic medications, weight gain is likely. There is a risk of glucose intolerance and, in older adolescents, galactorrhoea. However, these problems are more likely to emerge in adolescent patients receiving high doses of atypical antipsychotics to manage acute psychosis or mood disturbance.

Minimum investigations to be carried out in patients likely to receive risperidone should include growth parameters, but if feasible full blood count, liver enzymes, random blood glucose, serum prolactin (in older adolescents), and an ECG should also be obtained before commencing treatment. Drug education should include advice about dietary control and exercise. Restricting the child's access to snack food can be effective in limiting weight gain. At follow-up visits, the patient should be observed for abnormal movements and assessed for changes in muscle tone.

Problems of aggression fluctuate; therefore, it is important not to respond to each spike in behaviour with a dose increase. Carers can be encouraged to keep a diary to document the behaviour of the child or adolescent. This can be used to assess week-by-week variation in aggression and guide treatment decisions. Hour-by-hour variation in aggression is better addressed by attending to the child or adolescent's environment rather than by medications.

Other atypical antipsychotics and pericyazine (Neulactil) are prescribed for young people with aggression associated with autism or intellectual disability, but the evidence for efficacy is less robust. Clonidine monotherapy offers an alternative strategy for reducing arousal. Patients whose aggression arises in the context of OCD-like behaviour may respond to SSRIs.

Tic disorders

Tourette's syndrome and other chronic tic disorders are more likely to cause embarrassment than impairment. Associated problems, such as obsessionality or hyperactivity, may cause the patient most difficulty. Nevertheless, tic disorders can usually be suppressed with clonidine, low doses of high potency antipsychotics such as haloperidol (Serenace), or one of the atypical antipsychotics such as risperidone. Tic disorders fluctuate in intensity and frequency; therefore, a recurrence of tic symptoms following adequate suppression is not an automatic indication for a dose increase or a change in treatment. For patients who also have comorbid ADHD, clonidine or atomoxetine may be successful in suppressing the tic symptoms and hyperactive behaviours.

Juvenile onset bipolar disorder

Children and adolescents with bipolar affective disorder usually have severe and complex problems. GPs should only consider treating such patients if they have had specific training, or if they work in close collaboration with child mental health services. Pharmacological treatment typically comprises a mood stabiliser such as sodium valproate (Epilim, Valpro), lithium (Lithicarb, Quilonum SR), or lamotrigine augmented with one of the atypical antipsychotics. Antidepressant medications are avoided due to the risk of precipitating mania.

Lithium is the most effective treatment for preventing the recurrence of mania, but the need for regular blood tests to monitor serum levels limits its acceptability to many patients.

Sodium valproate, commencing at a dose of 10 mg/kg per day in two divided doses and titrated to a maximum of 50 mg/kg per day, is well tolerated by most patients. Side effects of sodium valproate include weight gain, sedation and dyspepsia. Rare but important adverse reactions include liver toxicity, pancreatitis, menstrual dysfunction and blood dyscrasia. Baseline investigations should include growth parameters, full blood count and liver function tests. Treatment with lamotrigine is best supervised by a specialist service owing to the risk of a severe life-threatening rash.

Psychosis

Psychotic-like symptoms in young people are as likely to arise from nonpsychotic conditions such as substance abuse, dissociative states, post-traumatic stress disorder and OCD as they are from schizophrenia or severe mood disorder. For this reason, specialist evaluation is recommended. Some young or intellectually disabled children who engage in antisocial behaviour will report that a voice in their head commanded them to act in that manner. Such children are usually describing their own thoughts.

True psychosis is managed with one of the atypical antipsychotic medications and the baseline assessment recommended above in the aggressive behaviour associated with autism section should be followed. Dose requirements are generally higher for psychosis than for aggression. If possible, young people with psychosis should participate in an early intervention program that attends to their social,

psychological and vocational needs.

Conclusion

Psychotropic medication is a useful tool to decrease distress and improve functioning in children and adolescents who have psychiatric disorders. Such medications are safe and effective provided clinicians follow good prescribing practice. Pharmacological treatment of uncomplicated OCD, anxiety and tic disorders can be undertaken by GPs who fully understand treatment options and side effects; however, other more complex or controversial disorders are better managed by specialist services. MT

Further reading

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DECLARATION OF INTEREST: Professor Hazell has participated in: speaker's bureau for Astra Zeneca; contract research for Celltech; advisory boards, submissions to drug regulatory and funding bodies, contract research, and speaker's bureau for Eli-Lilly; advisory board and speaker's bureau for Janssen-Cilag; advisory board for Novartis; speaker's bureau for Pfizer; advisory board for Shire.