Mental health care in the pediatric clinic

More psychopharmacology, including antipsychotics

Objectives

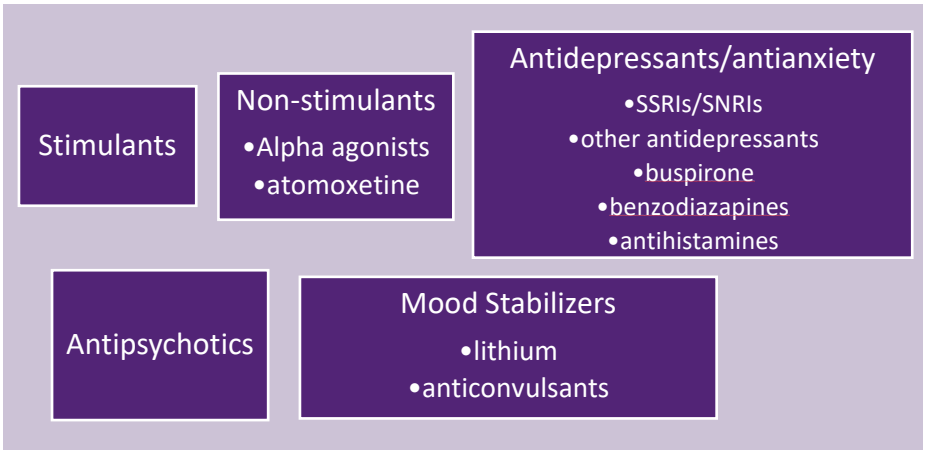
By the end of this chapter, you will be able to:

Identify less-commonly used medications for depression and anxiety

List indications for and risks associated with antipsychotic medications

Overview of psychopharmacologic classes

To the right are the major classes of medications used in psychiatry. We have covered the stimulants, non-stimulants for ADHD, and the SSRI and to some extent the SNRI antidepressant/anti-anxiety medications in sufficient detail for you to use them in routine care. You may have patients taking other psychotropic medications for various reasons, and it is helpful to know what these medications are, their indications, actions, side effects, and other concerns.



Other antidepressants (none FDA-approved in pediatrics)

Bupropion

- Used for depression, ADHD (third-line), smoking cessation
- Weight-neutral, non-sedating
- Contraindicated if seizure history or eating d/o as may lower seizure threshold

Mirtazapine

- Used for depression and anxiety
- May help with sleep onset
- Causes weight gain- may be beneficial for patients who need to gain weight

Trazodone

- Used for depression, and more often for sleep onset
- May cause orthostatic hypotension and rarely, priapism

Other anti-anxiety medications

Buspirone: serotonin 1A receptor partial agonist, not effective in pediatric trials, requires bid-tid dosing, minimal side effect profile

Benzodiazapines: have a role in inpatient settings or sedation for procedures, but they have no role in outpatient primary care mental health treatment. Trials of benzodiazepine medications for anxiety disorders in adolescents have shown no efficacy superior to placebo. Misuse and diversion of prescribed benzodiazepine medication is common.

Antihistamines: may be used scheduled or prn, limited by sedation or by paradoxical disinhibition

- diphenhydramine
- hydroxyzine
- cyproheptadine

A bit about sleep and mental health

Sleep problems are very common in children and adolescents with mental health disorders, as well as in those without.

Sleep hygiene is a critical part of the treatment of all sleep problems and many, if not all, mental health problems.

Screen for obstructive sleep apnea in patients with inattention, fatigue, or irritability.

There are many online patient handouts on sleep hygiene: pick one you like, ideally from a university-based site, and have it ready to review with families.

Electronic device use is often a problem. Children and adults do not sleep properly if they have electronic devices in or near their beds.

Medications for sleep:

Should be used sparingly, if at all, and only in conjunction with sleep hygiene

Will not work indefinitely

Will not override the will of a child who does not want to go to sleep

Are not FDA-approved for sleep in children

Avoid hypnotics and benzodiazapines for sleep in pediatric patients

Medications for help with sleep onset (none will help maintain sleep through the night):

Melatonin

- Effective in RCTs in children with ADHD, with autism
- Note that melatonin is a food supplement and not regulated by FDA

CONSIDER using a medication that meets more than one need:

- **antihistamines**: in a child with allergies and sleep problems, a sedating antihistamine can target both
- **alpha-agonists**: a child with ADHD and sleep problems who is using clonidine or guanfacine immediate release forms during the day can use a slightly higher dose at bedtime to help with sleep onset

Mood stabilizers

Mood stabilizers are not a class of medications, but simply medications used to treat mania, to serve as maintenance treatment in bipolar disorder, and sometimes in an off-label manner to treat severe aggressive behavior. Mood stabilizers include antipsychotics, which we will discuss later, lithium, and various anti-epileptic drugs with which you are likely familiar. The notes below highlight some aspects of each medication that you should be aware of if you have a patient taking it.

- Lithium
  - Highly effective for many patients with bipolar disorder
  - Offers some protection against suicidality
  - Must monitor renal and thyroid function, weight, baseline ECG
  - May worsen acne
  - Teratogenicity may be less than thought (cardiac)
- Depakote
  - Effective for many patients with bipolar disorder
  - Must monitor weight, liver function
  - Teratogenic; not recommended for teen females
- Other anticonvulsants
  - Lamotrigine: used for bipolar depression. Slow titration/risk of Stevens Johnson
  - Oxcarbazapine: less evidence of efficacy, well tolerated, less weight gain

Antipsychotics: overview

Typical (first generation antipsychotics, FGA)

- Rarely used, <10% of current prescriptions
- Haloperidol, thorazine, perphenazine

Atypical (second generation antipsychotics, SGA)

- Risperidone, quetiapine, aripiprazole, olanzapine, ziprasidone, clozapine, asenapine, paliperidone, iloperidone

The antipsychotic medications emerged in the 1960's and revolutionized the treatment of schizophrenia and other severe mental illness. Use was limited in part by severe and sometimes permanent movement disorders related to dopamine blockade in the basal ganglia. This first group of medications are referred to as typical or first generation antipsychotics, and now mostly superseded by the second generation or atypical antipsychotics. The atypicals, or SGAs, have been associated with more improvement in the negative symptoms of schizophrenia and with lower risk of severe movement disorders, but are associated with greater metabolic side effects. For the remainder of this discussion, we will focus on the second-generation antipsychotics.

Daphne

You are working at a weekly clinic that serves children in the local foster care system. Your 3rd patient is Daphne, a 12-year-old girl who has been in the system for 2 years and who was recently placed with an aunt who hopes to foster to adopt. Limited records indicate that Daphne is taking quetiapine 100 mg bid, and has been on this dose for 20 months, starting after an inpatient psychiatric stay. Since then the quetiapine appears to have been refilled by a series of providers. Daphne is unsure what the medication is for, other than "behavior". She says that when she was first removed from her mother's custody, at age 10, she would act out and fight with members of her first foster family. Daphne denies sustained depressed mood, thoughts of self-harm or harm to others, suicidal thoughts, or history of hallucinations. She is making B grades in her new school, has not had discipline problems at school, and is hopeful about life with her aunt.

On exam, Daphne has a body mass index of 26.4 and acanthosis nigricans on her neck and popliteal fossae.

What should you do about the quetiapine?

a) Continue the current prescription

b) Put Daphne on a waitlist to see a psychiatrist

c) Discontinue the medication today

d) Prescribe a scheduled taper off, following up with you

Before we answer the question about Daphne's quetiapine, let's take a look at the antipsychotics, their indications, risks, and side effects. As you can see below, the FDA has approved the use of atypical or second-generation antipsychotics in children for severe mental illness including schizophrenia and bipolar disorder. Aripiprazole has an indication for Tourette's Disorder, although alpha-agonists such as guanfacine and clonidine are more commonly used first line for Tourette's. Aripiprazole and risperidone have been approved for use in children with autistic disorder who manifest severe irritability and aggression. This latter use should always occur in conjunction with environmental modifications and behavioral therapy and should be considered temporary.

FDA pediatric indications for atypical antipsychotics

Schizophrenia
- risperidone, olanzapine, quetiapine, aripiprazole, lurasidone (age 13+ years), asenapine (age 12+ years)

Bipolar type 1 disorder, mixed or manic
- risperidone, quetiapine, aripiprazole, asenapine (age 10+ years)

Bipolar type 1 disorder, depressed
- olanzapine, lurasidone (age 10+ years)

Tourette's disorder
- aripiprazole, age 6+ years

Irritability with Autism Spectrum Disorder
- aripiprazole (age 6+ years), risperidone (age 5+ years)

Antipsychotics: side effects-metabolic/endocrine

Weight gain, diabetes, and hyperlipidemia are common with SGAs. Aggression around food-seeking behavior may emerge. Glucose and lipid changes may be related to increased appetite leading to increased food intake, or direct metabolic effects.

Hyperprolactinemia: may be associated with gynecomastia, galactorrhea, amenorrhea, oligomenorrhea, hirsutism, erectile dysfunction, decreased libido. Generally reversible with discontinuation of the drug. Aripiprazole, a partial D2 receptor agonist, actually decreases prolactin levels

The big concern with the now commonly prescribed antipsychotic medications is their potential to cause weight gain, increased blood sugar or disrupted glucose metabolism, and hyperlipidemias. These metabolic effects may be related simply to the tendency of the medications to increase appetite, in which case dietary and behavioral modifications may mitigate this, but there is evidence for more direct impact of the antipsychotics on metabolic pathways. In either case, children on long-term antipsychotics are at risk for obesity, hyperlipidemia, and insulin resistance. Daphne reports having been "skinny" as a younger child but having gained weight over the past 2 years.

Antipsychotics: side effects- other

Dystonia: stiffening or abnormal movements, often of face, neck, trunk. Rapidly reversible with oral or IM diphenhydramine.

Akathisia: sense of intense restlessness, unable to be still, acute change from baseline

Cardiac conduction changes: unclear if antipsychotic-associated prolongation of QTc is associated with increased risk of Torsade de Pointes, but baseline and monitoring ECG appropriate if positive family history, if on other meds that prolong QTc, or with ziprasidone

Tardive dyskinesia: Irreversible stereotypical orofacial or other movements

Other adverse effects of antipsychotics involve the neurologic and cardiac systems. Dystonia and akathisia often present early in treatment and require a change in medication or the addition of an additional medication such as benztropine to control dystonia or a beta blocker to control akathisia. ECGs are not routinely done prior to starting atypical antipsychotics other than ziprasidone but should be considered in a patient with a family history of prolonged QTc or other conduction abnormalities. Finally, tardive dyskinesia, which was the bane of the first generation antipsychotics, can still occur in patients taking high-potency second generation antipsychotics such as risperidone over long periods.

Adverse effect profile of commonly used SGAs

Adverse effect	**aripiprazole**	**lurasidone**	**olanzapine**	**quetiapine**	**risperidone**	**ziprasidone**
weight gain	0/+	0/+	+++	++	++	0/+
diabetes	0/+	0/+	+++	++	+	0/+
increased lipids	0/+	0/+	+++	++	+	0/+
increased prolactin	0/+	+	+	0	+++	+
sedation	0/+	+/++	+/++	++	+	+
extra-pyramidal effects (dystonias)	+	+/++	0/+	0	++	+
akathisia	++	+/++	+	+	+	+/++
0/+ = minimal effect + = mild effect ++ = moderate effect +++ = severe effect						

Adapted from C Correll in Dulcan's Textbook of Child and Adolescent Psychiatry, 2nd edition, APPI 2022

The American Diabetes Association and the American Psychiatric Association wrote consensus guidelines on monitoring for adverse metabolic changes. In addition to metabolic monitoring, patients should be monitored for the signs and symptoms of hyperprolactinemia, and if these are present, either stop the antipsychotic and monitor for remission of symptoms, or check prolactin level and if elevated, consider further work-up for non-medication-induced etiologies.

Metabolic monitoring parameters based on consensus guidelines

	Baseline	Week 4	Week 8	Week 12	Q 3 months thereafter	Annually
Medical history (personal and family h/o obesity, HTN, diabetes and CV disease)	X			X		X
Weight, height, BMI	X	X	X	X	X	X
Blood pressure	X			X		X
Fasting glucose/HbA1C	X			X		X
Fasting lipids	X			X		X

Antipsychotics: off-label use

- Antipsychotic off-label use is most commonly for aggressive behavior, often in children with ADHD.
- More commonly used:
    - in younger children
    - in children in foster care
    - in children with intellectual disability
    - in children covered by Medicaid
- Problems with use:
    - Often used for extended periods without concurrent appropriate behavioral therapy
    - Rarely accompanied by recommended metabolic monitoring
    - Represent a significant portion of pharmacy benefits costs in many health plans

The off-label use of antipsychotic medication in children increased dramatically beginning in the early 1990s, leveling off around 2008. Rates remain high, particularly among vulnerable populations including children in foster care, children with Medicaid, and children with intellectual disability. Despite recommendations, these medications are often used for extended periods to target behavior or symptoms without concurrent behavioral therapy or parent management training. This is particularly problematic when children whose behavioral problems are related to Post Traumatic Stress Disorder receive antipsychotics without trauma-focused cognitive behavioral therapy. Because of this, some states and some insurance plans have implemented oversight processes to review and curtail off-label antipsychotic prescribing to certain populations of children. These processes may be experienced as burdensome but would have probably triggered a review of Daphne's quetiapine prescription before she came to you.

A word about aggression

Aggression is a behavior.

It can be a symptom, but it is not a diagnosis.

Aggression most often emerges when a person lacks other cognitive, verbal, social, or emotional skills or resources to get his or her needs met.

A person can gain these skills and resources through coaching, seeing them modeled, specific therapies, and sometimes simply by maturing.

Pharmacotherapy to reduce aggression may decrease the impulsive, irritable urge to aggression, but does not replace the aggressive behavior with adaptive behaviors.

Kids just get mad.

Some get mad more often, for longer, with more severe and destructive consequences than do others.

We cannot expect any child to behave better than the most poorly behaved adult in their home.

We know that temper tantrums are normal in 2- and 3-year-olds and tend to decrease with time as children develop the skills to communicate their needs, work through challenges, manage frustration, and find that waiting for things is tolerable. Some children have delays or deficits in this area of development. If an older child is still having rages and tantrums, one question is, "Who else acts like this at home?" If an adult, or even an older sibling, regularly models dysregulated behavior, it can be very difficult for the child to learn to regulate his own. In these cases, treatment must involve changing the behavior of the model.

Aggression and ADHD

Some children with ADHD also have aggressive behavior

This aggression is related to impulsivity; acting on the aggressive urge before being able to think through consequences and alternatives.

It can also be related to frustration around constant redirection.

The most effective treatment is assertive ADHD treatment, using stimulants and sometime non-stimulants to maximum potential.

In children with ADHD and residual aggression despite assertive ADHD treatment, augmentation with mood stabilizers (valproate) or atypical antipsychotics has been shown effective in randomized controlled trials.

That said, such augmentation should be used judiciously and in a time-limited manner with ongoing behavioral therapy.

What happened to Daphne?

We don't know exactly.

We can speculate that being 10 years old and removed from her mother's care was frightening and upsetting.

We know that anxiety and fear can present with irritability and aggression, and it sounds like that happened with Daphne.

She may have felt that lashing out would get her out of her situation and back to her mom.

There is no evidence that Daphne has or had schizophrenia, bipolar disorder, autism, or Tourette's disorder.

In any event, she was hospitalized, started on an atypical antipsychotic off-label for aggressive behavior in a neurotypical child, and has continued on it.

Does Daphne need medication now?

In our Conceptual Framework chapter, we said that mental health includes:

- Learning to regulate feelings and behavior, and tolerate distress
- Being able to form and maintain relationships
- Developing a sense of right and wrong
- Being able to play and attain developmental milestones

Pertinent negatives include:

- Lack of dangerousness to self or others
- Lack of psychotic symptoms including hallucinations or delusions

Just as you can quickly conduct a well child check and through a brief history and physical determine that a child has no current disease, you can briefly assess a child for mental wellness. Daphne is successfully attending school, meeting educational goals, has no major disciplinary issues, is loved and wanted by her aunt, and is optimistic about her future. You have checked off the pertinent negatives in that she has no thoughts or behaviors indicating danger to self or others, or any history of psychotic symptoms. This does not mean that she might not have grief for her mother, or anxiety about her future, but you can see that she has no condition which is an indication for treatment with an antipsychotic medication.

Antipsychotics: how long to treat?

(For conditions other than schizophrenia and bipolar disorder type 1)

No child should be treated with an antipsychotic for an off-label indication "indefinitely".

How long do we treat children with antipsychotic medications prescribed off label? For as long as needed to achieve a level of emotional and behavioral regulation that allows the child to function in home and school environments and to work in therapy to develop the skills needed to achieve that regulation without the medication. How will you know when you have gotten to that point? Get the child to a position of stability and taper the medication off and assess for ongoing or residual symptoms. Restarting the medication should only occur if symptoms recur at a level that markedly interferes with the child's functioning. No child should be treated with an antipsychotic for an off-label indication indefinitely.

Antipsychotics: stopping

Taper off.

There is little evidence on best practice.

Consider decreasing by 25% of the dose every 7-10 days until gone; smaller increments may be appropriate for higher doses.

The tapering time serves in part allowing the child and family to observe behavioral responses to stopping the medication in a gradual way. There are generally not discontinuation symptoms associated with atypical antipsychotics with the rare exception of withdrawal dyskinesia associated with the rapid discontinuation of high dose, high potency antipsychotics. Withdrawal dyskinesia presents as bizarre, often athetoid movements. Treatment: go back to previous dose and taper more slowly.

Daphne

You recommend that Daphne decrease the quetiapine by 50 mg/dose every 10 days:

- 50 mg q am and 100 mg q pm for 10 days
- 50 mg bid for 10 days
- 50 mg at night only for 10 days
- Stop

Daphne returns in 3 months. She is no longer taking quetiapine. She is feels brighter and less tired. Her BMI has dropped 1.2 points. Her aunt has no concerns, and the adoption is going through.