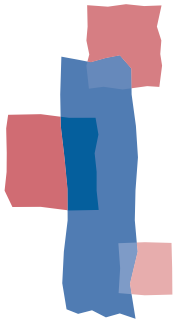

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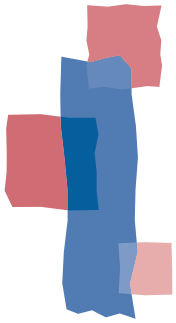

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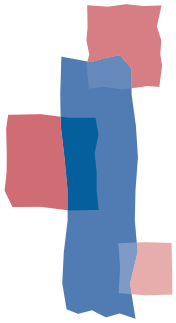

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Medication Management

This booklet covers medications available to youths with disruptive behavior disorders (DBDs). The information will help child-caring agencies understand what medical treatment options exist and how to prevent the inappropriate use of antipsychotic medications with children and youth.

Interventions for Disruptive Behavior Disorders

For additional references on interventions for disruptive behavior disorders, see the booklet, *Evidence-Based and Promising Practices*.

This KIT is part of a series of Evidence-Based Practices KITs created by the Center for Mental Health Services, Substance Abuse and Mental Health Services Administration, U.S. Department of Health and Human Services.

This booklet is part of the Interventions for Disruptive Behavior Disorders KIT, which includes six booklets:

How to Use the Evidence-Based Practices KITs

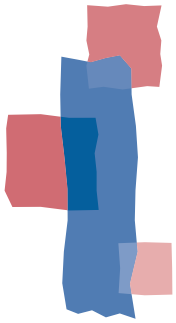
Characteristics and Needs of Children with Disruptive Behavior Disorders and Their Families

Selecting Evidence-Based Practicess for Children with Disruptive Behavior Disorders to Address Unmet Needs: Factors to Consider in Decisionmaking

Implementation Considerations

Evidence-Based and Promising Practices

Medication Management



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Medication Management

Introduction

As noted in *How to Use the Evidence-Based Practices KITs*, no specific evidence-based medication algorithms exist (meaning systematic steps for physicians to consider in selecting medications) for treating disruptive behavior disorders (DBDs). While the concept of evidence-based practice (EBP) has been present in the mental health literature for more than 15 years, it has not been used frequently in the medical literature on mental health.

In the absence of controlled clinical trials, the judgments of individual clinicians often become the basis for the standards by which medications are assessed for effectiveness. These judgments give rise to a consensus in the field. This is the case for many psychopharmacologic interventions.

Further complicating the evidence base for medications used for treatment of psychological disorders is the fact that many of the medications used to treat DBDs are often "off label," meaning that the medications are used in a manner that was not identified in the initial clinical trials or in the approvals from the U.S. Food and Drug Administration (FDA).

Traditionally, studies that have been undertaken have focused on using psychopharmacologic interventions for specific disorders. More recently, however, studies have focused on the symptoms that are key hallmarks of these disorders. For example, studies in the past have focused on treatment for specific DBDs such as Conduct Disorder, while more recent studies have looked at treatment for aggression.

This booklet focuses on medical interventions for both the specific disruptive behavior disorders and aggressive behavior, which is the hallmark of all of the DBDs.

The most widely studied medications for DBDs fall into the following categories:

- Atypical antipsychotics (risperidone, quetiapine, aripiprizole, olanzapine);
- Mood stabilizers (valproic acid, lithium); and
- Alpha agonists (clonidine, guanfacine).

Atypical (Second Generation) Antipsychotic Medications

Maladaptive aggression is the hallmark for most of the DBDs. In fact, aggression is the primary reason for referral to child psychiatric clinics in the United States, and much of the aggression has been associated with DBDs.

While it is clear that maladaptive aggression is not limited to the DBDs, the level of co-morbidity (the appearance of both) suggests that there is a strong association between aggression and the DBDs. As a result, researchers have begun looking at the symptoms such as aggression as the focus of treatment rather than at the disorders themselves.

Although atypical antipsychotic medications have been used to treat aggressive behaviors for years, research has been limited in this area. (*Atypical* and *second-generation* can be confusing to lay people. They simply mean these medications were developed after the first generation of psychiatric medications. At one time it was "atypical" to use these medications, but their use has become more common.)

Many of the studies that have formed the basis of the evidence for this commonly increasing practice are case studies and small, less sophisticated studies. Relatively few controlled studies exist at this time, although the numbers are increasing.

The drugs in this category that have been studied in relation to DBDs include risperidone, quetiapine, aripiprazole, ziprasidone, olanzapine, and clozapine. Although the physiological basis for using these medications to treat aggressive behavior is unclear, the current evidence suggests that they act through their effect on the serotonin and dopamine neurotransmitter systems.

These medications were first approved as a treatment for psychotic disorders. The symptoms of psychosis that have been treated with these medications include hallucinations (hearing voices or seeing things that are not there) and delusions (beliefs that are not based in reality).

Atypical antipsychotic drugs studied for effects on DBDs

- Risperidone
- Quetiapine
- Aripiprazole
- Ziprasidone
- Olanzapine
- Clozapine

Further study has shown that these medications also have several other positive effects beyond the treatment of psychosis. These medications have been shown to reduce severe aggression and behavioral problems in youth with DBDs. They also act as mood stabilizers, which help reduce mood swings as well as decrease symptoms of mania and depression in youth.

A few caveats must be considered when prescribing these medications to youth. Most of the studies using these medications involved adults. Relatively few studies were conducted with adolescents and even fewer studies with younger children.

Also, significant side effects are associated with this class of drugs. Because of these side effects, it is important for people to be closely monitored by a physician. Before starting treatment, the youth should have a thorough physical examination to identify and address any preexisting medical conditions. This will include monitoring the youth's weight, heart rate, and blood pressure. The doctor will likely order several blood tests, including a baseline blood sugar level and cholesterol level.

It is important for these lab tests to be checked every few months to make sure that the medications are not having any negative side effects, most commonly weight gain and sometimes sedation.

As a general rule, these medications' side effects can be adequately addressed without long-term consequences, as long as the medications are being carefully monitored by the physician.

Another test, which should occur at the initiation of these medications, is the Abnormal Involuntary Movement Scale (AIMS). This test will involve the physician visually monitoring the youth for any movements in the youth's tongue, face, legs, and arms. Other potential side effects, generally thought to be rare, include changes in blood sugar, increased cholesterol levels, and early onset diabetes.

It is important that the doctor repeat this examination every few months to make sure that the youth is not developing any abnormal movements. The most serious of these movement disorders is called *tardive dyskinesia* and is characterized by abnormal and uncontrollable body and facial movements. These movements may be very subtle but may also appear as sudden, jerking movements.

Although these symptoms do not usually appear until a person has been on these medications for several months to years, it is important to monitor them closely because they are often irreversible.

Table 1 includes a list of potential side effects associated with atypical antipsychotics. The youth's physician should be made immediately aware if any of these symptoms arise. For the rare and serious side effects, it is important to address these symptoms immediately, and 911 should be called.

The best source of information about an individual youth is the physician prescribing the medications. A thorough discussion of the potential side effects and the method for handling these side effects should occur at the time that the medications are prescribed.

Table 1: Side Effects Associated with Atypical Antipsychotics

Common	Rare	Rare and serious (Call 911)
Sedation	Dry mouth	Tardive dyskinesia
Insomnia	Dizziness	Allergic reactions (for example, trouble breathing, swelling of lips and tongue)
Headache	Restlessness	
Nausea	Tremor, muscle stiffness	Frequent thirst or urination
Increased appetite (weight gain)	Slow movements, movement problems	Sudden stiffness or high fever

Mood Stabilizers

Mood stabilizers, including valproic acid, carbamazepine, and lithium, have demonstrated efficacy in reducing aggressive behaviors in adolescents with DBDs. Valproic acid and carbamazepine have a long history in the treatment of seizure disorder and these two medications, along with lithium, have a long-standing history in the treatment of Bipolar Disorder.

More recent evidence has shown that they are also effective agents for decreasing the level of impulsivity and aggression in people with DBDs.

Mood stabilizing drugs studied for effects on DBDs

- Valproic acid
- Carbamazepine
- Lithium

As with the atypical antipsychotic medications, these medications require ongoing safety monitoring. Although these medications are classified as a single group for the purposes of this presentation, the side effect profiles differ.

Before prescribing these medications, it is important that a thorough medical history be obtained and that the youth has a physical examination to identify preexisting medical conditions. Valproic acid and carbamazepine are associated with weight gain, blood disorders, and potential liver problems, which must be closely monitored. Lithium is associated with fatigue, enuresis, nausea, vomiting, increased thirst, and weight gain.

Baseline laboratory monitoring should be completed before the initiation of these medications and at specified intervals after the initiation to monitor and prevent negative side effects.

Unlike the previous medications, each of these drugs has a therapeutic "window." This therapeutic window is the level of drug in the body at which the drug works optimally. This therapeutic window is monitored through blood testing, which will initially be performed about once a month, with this interval decreasing until monitoring occurs once per 6 months to a year after the youth is stable on the medication. Additionally, monitoring liver functioning, as well as monitoring white blood cell count, is indicated for carbamazepine, as it may reduce white blood cells and platelets, placing the youth at risk for infection and bleeding problems if not adequately monitored. Lithium can negatively affect the kidneys and thyroid as well as bone marrow activation. These areas must be monitored through medical laboratory testing.

It is important that potential risks and benefits be discussed with the youth and family so that an appropriate informed decision can be made. The side effects associated with these medications are presented in Tables 2 and 3.

Table 2: Side Effects Associated with Mood Stabilizers

Common	Rare	Rare and Serious
Sedation	Dry mouth	Liver problems
Dizziness	Dizziness	Bone marrow suppression—decreased white blood cell count (Tegretol brand of carbamazepine only)
Headache	Restlessness	Pancreatitis
Nausea, vomiting, indigestion	Migraine headaches	Problems with blood clotting
Increased appetite (weight gain)	Rash, itching	Sudden stiffness or high fever
Tremor	Hair loss	Severe allergic reactions (for example, trouble breathing, swelling of lips and tongue)
Constipation	Hives	

Table 3: Side Effects Associated with Lithium

Common	Rare	Rare and Serious
Sedation	Muscle weakness	Hypothyroidism (temperature sensitivity, weight gain, hoarseness, decreased energy)
Insomnia	Dizziness	Increased white blood cell count
Headache	Restlessness	Muscle weakness
Nausea, vomiting, diarrhea	Tremor	Frequent thirst or urination
Increased or decreased appetite	Rash, itching	Lithium toxicity (Sudden onset of tremor, nausea, vomiting)

Alpha Antagonists

The medications in this category that are most often used to treat youth are clonidine and guanfacine. These medications are effective in treating impulsive behaviors and aggression associated with DBDs, but they have the potential for adverse side effects. These medications have been used with youth who have a history of aggression, temper tantrums, and fighting.

Mood stabilizing drugs studied for effects on DBDs

- Clonidine
- Guanfacine

These medications have FDA approval in treating hypertension in adults. Clinicians must therefore exercise great care when prescribing these medications to youth because there is the risk of decreasing blood pressure to dangerously low levels. In addition to potential hypotensive episodes, one must also be aware of syncopal (decreased blood pressure leading to loss of consciousness) episodes as well as cardiac problems, which may also be associated with the using these medications. Many of the side effects that are more common in adults are less common in youth (for example, hypotension).

Side effects should be thoroughly discussed with the physician at the time that the medication is prescribed so that both the youth and family are aware of them and how they will be handled if they arise.

Any side effects should be reported to the physician at once. It is important that the medication not be discontinued abruptly because of the risk of rebound hypertension, which results in a potentially dangerously high blood pressure. Side effects associated with these medications are shown in Table 4.

Table 4: Side Effects Associated with Alpha Blockers

Common	Rare	Rare and Serious
Sedation	Confusion	Severe dizziness
Hypotension	Nocturnal enuresis (bedwetting)	Irregular heartbeat
Headache	Muscle cramps	Difficulty urinating
Stomachache	Tremor	Fainting
Lightheadedness, dizziness	Rash, itching	Trouble breathing
Decreased pulse rate	Runny nose	Swelling of lips and tongue

Other Medications

Treating aggression is challenging, and clinicians will often use second-line medications in treating aggression associated with DBDs. Second-line agents are medications that are used to treat DBDs where the initial treatment/medication fails.

A number of medications have been used to treat DBDs in the past but are no longer first- or second-line agents. This is due to unfavorable possible side effects and the introduction of newer medications with greater efficacy and more favorable side effect profiles.

Before the advent of the atypical antipsychotic agents, the older antipsychotic medications including haloperidol and molindone were used to treat aggressive behaviors in youth with Conduct Disorder. Although these medications had demonstrated efficacy in double-blind studies for treating aggression in youth with Conduct Disorder, numerous potential side effects existed, including tardive dyskinesia and neuroleptic malignant syndrome. Although these medications are not used as first-line agents in treating aggressive behavior, they remain viable alternatives for treating aggression.

Older agents such as tricyclic antidepressants have been used to treat aggressive behavior. These medications are no longer used frequently to treat aggressive behavior due to their level of side effects, including sedation, cardiac conduction delays, urinary hesitancy, and dry mouth.

Beta blockers can have significant side effects, including sedation, hypotension, bradycardia, and bronchoconstriction in children with asthma, which limit their utility in treating youth.

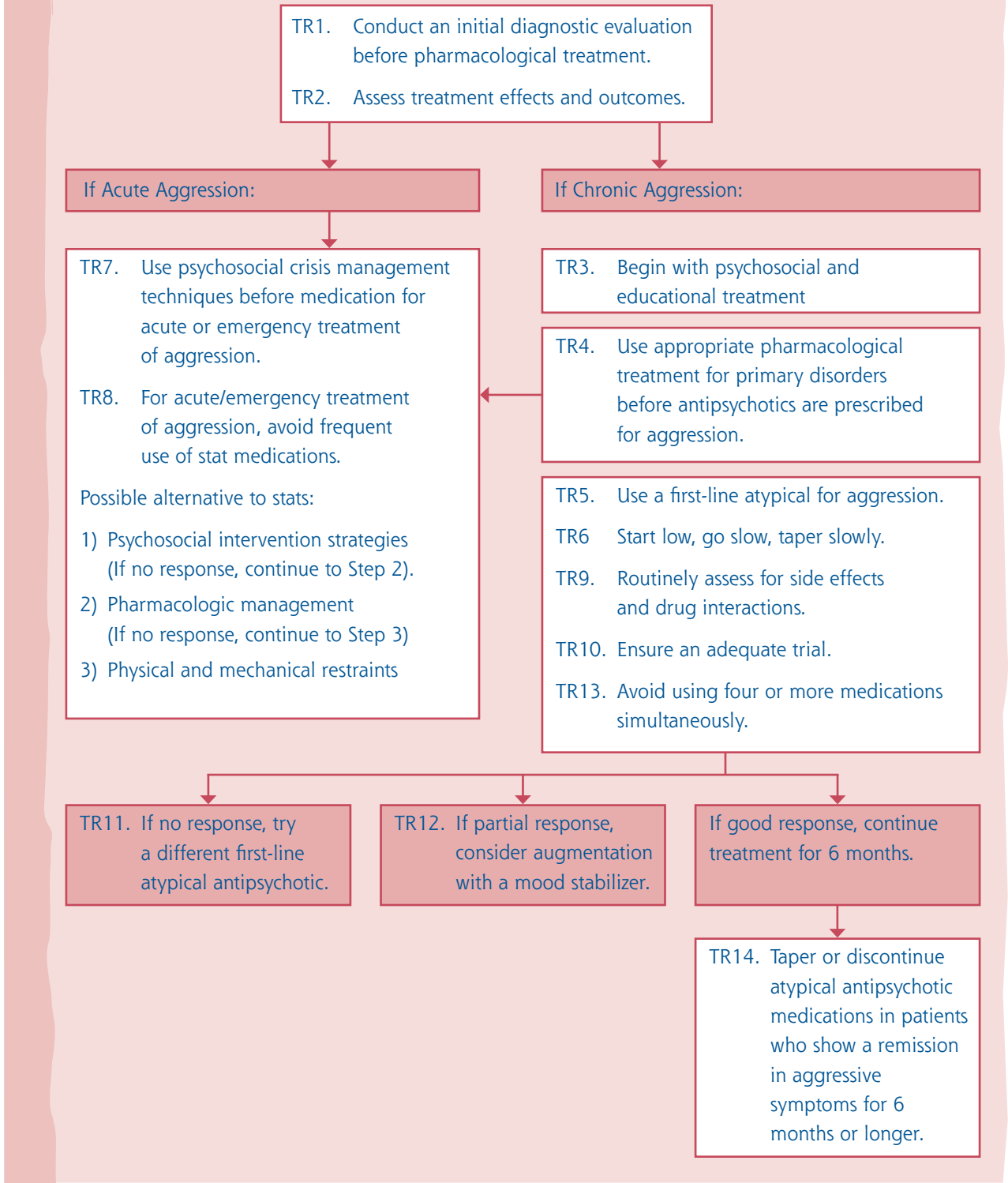
Recommendations

The Treatment Recommendations for the Use of Antipsychotics for Aggressive Youth (TRAAY) used the available evidence to develop guidelines to treat youth with aggressive behaviors. The guidelines were based on expert clinical consensus, as well as the available evidence in the research literature. These recommendations did not consider the diagnosis of the youth, but many of the youth met criteria for DBDs. The 14 treatment recommendations are presented in Figure 1.

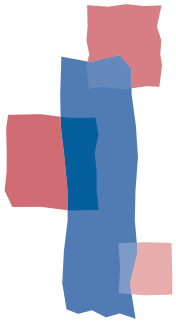
The goal of TRAAY was to develop guidelines to prevent the inappropriate use of antipsychotic medications for aggressive symptoms. While no evidence exists that this systematic approach will improve treatment outcomes, it represents the best integration of evidence-based practice for this population to date. It provides a method for emphasizing symptoms based on the best available current evidence, rather than emphasizing diagnoses, which may lead to unsuccessfully following a constellation of symptoms.

It is important to realize that the evidence for using these medications continues to expand. Also, the information used to prescribe these medications for youth with DBDs is not as strong as it is for many of the psychosocial interventions presented in this KIT. Much work remains to be done before these important disorders can be fully addressed.

Figure 1: Treatment Recommendations for the Use of Antipsychotics for Aggressive Youth



TR=Treatment Recommendation. See *TRAAY Pocket Reference Guide* by P. S. Jensen, J. C. MacIntyre, and E. A. Pappadopulos, 2004, New York, NY: State Office of Mental Health and Center for the Advancement of Children's Mental Health at Columbia University, Department of Child and Adolescent Psychiatry.



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