

# Recommendations for Cardiovascular Evaluation and Monitoring of Children and Adolescents Receiving Medications for ADHD

## Introduction

The American Heart Association (AHA) released a scientific statement and recommendations for cardiovascular monitoring of children and adolescents with heart disease receiving medications for ADHD on April 21, 2008. Subsequent controversy and conflicting interpretations of the statement soon led to a joint advisory from the AAP and AHA in an effort to clarify the recommendations. This joint statement is in its entirety below,<sup>1</sup> followed by the AHA's recommendations for (1) identifying children and adolescents at risk of sudden cardiac death, and (2) monitoring those who are on medications for ADHD. The accompanying table (Table 3) shows the cardiac effects of medications used to treat ADHD.

## American Academy of Pediatrics/American Heart Association Clarification of Statement on Cardiovascular Evaluation and Monitoring of Children and Adolescents With Heart Disease Receiving Medications for ADHD

***Endorsed by the American Academy of Child and Adolescent Psychiatry, the American College of Cardiology, Children and Adults with Attention-Deficit/Hyperactivity Disorder, the National Initiative for Children's Healthcare Quality and the Society for Developmental and Behavioral Pediatrics***

The American Heart Association released on April 21, 2008 a statement about cardiovascular evaluation and monitoring of children receiving drugs for the treatment of Attention Deficit Hyperactivity Disorder (ADHD). As a result of language in the news release and the statement as published, there have been conflicting interpretations of the recommendations regarding the use of an electrocardiogram (ECG) in assessing children with ADHD who may need treatment with medications. The purpose of this joint advisory of the American Academy of Pediatrics (AAP) and the American Heart Association (AHA) is to clarify the recommendations.

- The scientific statement included a review of data that show children with heart conditions have a higher incidence of ADHD.
- Because certain heart conditions in children may be difficult (even, in some cases, impossible) to detect, the AAP and AHA feel that it is prudent to carefully assess children for heart conditions who need to receive treatment with drugs for ADHD.
- Obtaining a patient and family health history and doing a physical exam focused on cardiovascular disease risk factors (Class I recommendations in the statement) are recommended by the AAP and AHA for assessing patients before treatment with drugs for ADHD.
- Acquiring an ECG is a Class IIa recommendation. This means that it is reasonable for a physician to consider obtaining an ECG as part of the evaluation of children being considered for stimulant drug therapy, but this should be at the physician's judgment, and it is not mandatory to obtain one.
- Treatment of a patient with ADHD should not be withheld because an ECG is not done. The child's physician is the best person to make the assessment about whether there is a need for an ECG.
- Medications that treat ADHD have not been shown to cause heart conditions nor have they been demonstrated to cause sudden cardiac death. However, some of these medications can increase or decrease heart rate and blood pressure. While these side effects are not usually considered dangerous, they should be monitored in children with heart conditions as the physician feels necessary.

The statement has been revised to clarify the language and to assure that the intent is clear to all readers. This is available at: <http://circ.ahajournals.org/cgi/reprint/CIRCULATIONAHA.107.189473>

The correction notice is at: <http://circ.ahajournals.org/cgi/content/full/CIRCULATIONAHA.107.189473/DC1>.

This clarification has been endorsed by the American Academy of Child and Adolescent Psychiatry, the American College of Cardiology, Children and Adults with Attention-Deficit/Hyperactivity Disorder, the National Initiative for Children's Healthcare Quality and the Society for Developmental and Behavioral Pediatrics.

<sup>1</sup> <http://www.newsroom.heart.org/index.php?s=43&item=398>



## Recommendations for Identifying Children and Adolescents at Potential Risk of Sudden Cardiac Death<sup>2</sup>

1. Patient and family history (class I, level of evidence C). The patient history should include questions to elicit the following:

- History of fainting or dizziness (particularly with exercise).
- Seizures.
- Rheumatic fever.
- Chest pain or shortness of breath with exercise.
- Unexplained, noticeable change in exercise tolerance.
- Palpitations, increased heart rate, or extra or skipped heart beats.
- History of high blood pressure.
- History of heart murmur other than innocent or functional murmur or history of other heart problems.
- Intercurrent viral illness with chest pains or palpitations.
- Current medications (prescribed and over the counter).
- Health supplements (nonprescribed).

The family history should include questions to elicit family history of any of the following:

- Sudden or unexplained death in someone young.
- SCD or “heart attack” in members <35 years of age.
- Sudden death during exercise.
- Cardiac arrhythmias.
- HCM or other cardiomyopathy, including dilated cardiomyopathy and right ventricular cardiomyopathy (right ventricular dysplasia).

- LQTS, short-QT syndrome, or Brugada syndrome.
- WPW or similar abnormal rhythm conditions.
- Event requiring resuscitation in young members (<35 years of age), including syncope requiring resuscitation.
- Marfan syndrome.

2. Physical examination (class I, level of evidence C). The physical examination should include an evaluation of the child for the presence of the following:

- Abnormal heart murmur.
- Other cardiovascular abnormalities, including hypertension and irregular or rapid heart rhythm.
- Physical findings suggestive of Marfan syndrome.

3. ECG (class IIa, level of evidence C). A baseline ECG, which often can identify cardiovascular abnormalities (eg, HCM, LQTS, and WPW anomaly), is reasonable to obtain. It is acknowledged that an ECG will not identify all individuals with the cardiac conditions noted above. It can be useful and can increase the sensitivity of the evaluation, especially if there are suspicions of high-risk conditions.

If possible, ECGs should be read by a pediatric cardiologist or a cardiologist or physician with expertise in reading pediatric electrocardiograms.

Once medication is started, if the initial ECG was obtained before the child was 12 years of age, developmental factors associated with puberty may warrant consideration of a repeat ECG. A similar situation is the development of new symptoms or a change in family history after the initial ECG was obtained, in which case a repeat ECG may be useful (class IIa, level of evidence C).

4. Pediatric cardiology consult (class I, level of evidence C). A consultation from a pediatric cardiologist should be obtained before the stimulant medication is started if there are any significant findings on physical examination, ECG, or history (such as known structural heart disease, arrhythmias, or a family history of SCD in members <35 years of age).

<sup>2</sup> Vetter, Victoria L., et al. “Cardiovascular Monitoring of Children and Adolescents With Heart Disease Receiving Medications for Attention Deficit/Hyperactivity Disorder.” *Circulation* 2008; 117: 2407-2423.



## Recommendations for Administration of Medications and Monitoring<sup>3</sup>

The consensus of the committee is that it is reasonable to obtain ECGs as part of the evaluation of children being considered for stimulant drug therapy. We recognize that there are no clinical trials to inform us on this topic and that there is variance in opinion on this topic. There are no widely accepted recommendations or standards of care for cardiac monitoring on stimulant medications. It is not known if the risk of SCD on stimulants is higher than in the general population or that the approach described will decrease the risk. However, the recent information and warnings regarding cardiac disease warrant reconsideration of the previous approach and thus the recommendations noted in this statement.

### Continuing Assessment

#### *Recommendations for Cardiovascular Monitoring of Patients on Specific Drugs*

1. Continuing assessment of patients should be made by the pediatrician at each visit by physical examination and by questions regarding potential cardiac symptoms and new family history. Findings should be noted in the history (class I, level of evidence C).
2. Blood pressure and pulse should be evaluated during routine follow-up within 1 to 3 months and at follow-up visits every 6 to 12 months for all medications and more frequently during titration and weaning of the agonists (class I, level of evidence C).
3. Any cardiac symptoms should result in appropriate referral and testing to determine whether any serious cardiac side effects are present (class I, level of evidence C).
4. Patient monitoring for specific drugs both before and after stimulant drugs are started is shown in Table 3.

#### *Recommendations for Cardiovascular Monitoring of Patients with Structural Heart Disease or Other Heart Conditions*

1. Although concerns have been raised in the drug monographs regarding all individuals with structural heart disease, there are no clinical studies or data indicating that children with most types of congenital heart disease are at significant risk for SCD while on these medications. It is reasonable to consider the use of stimulant medication in patients with congenital heart disease that is not repaired or repaired but without current hemodynamic or arrhythmic concerns or congenital heart disease that is considered to be stable by the patient's pediatric cardiologist unless the patient's pediatric cardiologist has specific concerns (class IIa, level of evidence C).
2. It is reasonable to use stimulants with caution in the following groups of patients (A through G) after other methods of treatment for ADHD have been considered or used (class IIa, level of evidence C).
3. Careful monitoring should be performed after initiation of stimulant medications in the following groups (A through G) (class I, level of evidence C).
  - A. Heart condition associated with SCD (LQTS, short-QT syndrome, HCM, arrhythmogenic right ventricular dysplasia, Brugada, coronary anomaly, WPW, Marfan syndrome).
  - B. History of an arrhythmia requiring cardiopulmonary resuscitation, direct current cardioversion or defibrillation, or overdrive pacing.
  - C. History of an arrhythmia associated with death or SCD.
  - D. Previous aborted SCD.
  - E. Other clinically significant arrhythmia not treated or controlled.
  - F. QTc on ECG \_\_\_\_\_ 0.46 seconds.
  - G. Heart rate or blood pressure \_\_\_\_\_ 2 SD above means for age.
4. If any of the above conditions or arrhythmias are diagnosed during treatment, consideration should be given to discontinuation of the stimulant medication until further testing and treatment can be achieved (class I, level of evidence C).
5. If arrhythmias are treated and controlled, on approval of a pediatric cardiologist, the patient can be restarted on medication (class I, level of evidence C).

<sup>3</sup> Vetter, Victoria L., et al. "Cardiovascular Monitoring of Children and Adolescents With Heart Disease Receiving Medications for Attention Deficit/Hyperactivity Disorder." *Circulation* 2008; 117: 2407-2423.

| Table 3. Cardiac Effects of Medications Used to Treat ADHD                             |  |  | Recommendations for Cardiovascular Monitoring               |  |
|--|--|--|---|--|
| Medications  | Mechanism of Action  | Cardiac Effects and Comments   | Class I, Level of Evidence C                                | Class IIa, Level of Evidence C   |
| Methylphenidate (Ritalin, Ritalin SR, Concerta, Metadate, Methylin, Focalin, Daytrana) | Release and/or inhibit reuptake of catecholamines (eg, D and NE) increase level of these NT at the synapse <sup>94</sup> | Increased HR and BP, no ECG changes <sup>107</sup>   | BP, HR  | ECG on first visit   |
| Amphetamine (Dextroamphetamine, Dextrostat, Adderall, Vyvanse)                         | Release and/or inhibit reuptake of catecholamines (eg, D and NE) increase level of NT at the synapse <sup>94</sup>       | Increased HR and BP, no ECG changes <sup>107</sup>   | BP, HR  | ECG on first visit   |
| Atomoxetine (Strattera)  | Selective norepinephrine reuptake inhibitor <sup>122</sup>   | Increased HR and BP in adults and children, palpitations in adults, no ECG changes <sup>122, 154, 155</sup>              | BP, HR <sup>91, 155</sup>                                   | ECG on first visit <sup>91, 155</sup>  |
| Clonidine (Catapres)   | $\alpha_2$ -Adrenergic agonist   | Decreased HR and BP, no ECG changes, <sup>130</sup> rebound hypertension with abrupt discontinuation <sup>133, 134</sup> | BP, HR; additional BP when medication is started and weaned | ECG on first visit   |
| Guanfacine (Tenex)   | $\alpha_2$ -Adrenergic agonist   | Decreased HR and BP, no ECG changes <sup>125, 156</sup>  | BP, HR  | ECG on first visit   |
| <b>Medications Not FDA Approved</b>  |  |  |   |  |
| Desipramine, imipramine  | Block the reuptake of D and NE   | Prolongation of QTc, PR, QRS, tachycardia <sup>143</sup> ; rare reports of sudden death <sup>46, 141</sup>               | BP, HR  | Baseline ECG and at dose increases<br>PR $\leq$ 200 ms<br>QRS $\leq$ 120 ms<br>QTc $\leq$ 460 ms |
| Bupropion (Wellbutrin, Zyban)  | Decreased firing rate of NE- and S-releasing neurons   | Increased BP in adults <sup>136</sup> (not in children <sup>135</sup> ) cardiac toxicity with overdose                   | BP, HR  | ECG on first visit <sup>132</sup>  |

D indicates dopamine; NE, norepinephrine; NT, neurotransmitter; HR, heart rate; BP, blood pressure; and S, serotonin.

Note: Drugs listed on this tool do not appear in any order of importance. The appearance of the names American Academy of Pediatrics, Quality Improvement Innovation Network, and National Initiative for Children's Healthcare Quality does not imply endorsement of any product or service. The recommendations in this publication do not indicate an exclusive course of treatment or serve as a standard of medical care. Variations, taking into account individual circumstances, may be appropriate. Original document included as part of *Caring for Children With ADHD: A Resource Toolkit for Clinicians*, 2nd Edition. Copyright © 2012 American Academy of Pediatrics. All Rights Reserved. The American Academy of Pediatrics does not review or endorse any modifications made to this document and in no event shall the AAP be liable for any such changes.