



### **ADHD: an Imbalance of Fire over Water**

In 493 BC, Hippocrates identified a condition that seems compatible with what is now called ADHD. He described patients who had “quicken responses to sensory experience, but also less tenaciousness because the soul moves on quickly to the next impression.” Hippocrates attributed this condition to an “overbalance of fire over water.”

The condition we refer to as “ADHD” dates to the mid-twentieth century, when physicians developed a diagnosis for a set of conditions variously referred to as “minimal brain damage”, “learning/behavioral disabilities” or “hyperactivity.” Estimates suggest that ADHD affects 3 percent to 7 percent of school-aged children and approximately 4 percent of adults. The three main symptoms of ADHD are inattention, hyperactivity, and impulsivity. People with ADHD may have difficulty in school, conduct problems leading to troubled relationships with family and peers, and run a higher risk of abusing drugs.

### **To Use or Not to Use ADHD Medications**

There seems to be both praise and concern for ADHD medications.<sup>1</sup> According to Steven Galson, Director, Center for Drug Evaluation and Research (CDER), “Medicines approved for the treatment of ADHD have real benefits for many patients but they may have serious risks as well.”

In the wake of public outrage at drug companies attempting to conceal adverse drug effects, the FDA created a new website providing drug safety information (<http://www.fda.gov/cder/drugSafety.html>). The following information about ADHD medications was on the FDA's new website. Adderall (extended release) was linked to 20 sudden deaths-14 in children. Concerta (methylphenidate, much like Ritalin) was linked to

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<sup>1</sup> FDA approved ADHD medications include: Adderall, Adderall XR, Concerta, Daytrana, Ritalin and Strattera.

difficulty breathing, irregular, fast heart beat, high blood pressure, and liver damage. Strattera (atomoxetine) an antidepressant, was linked to high systolic blood pressure, tachycardia, hypotension, abdominal pain, nausea, vomiting and mood swings.

A Washington Post article reported on a study published in the journal of *Drug and Alcohol Dependence* which estimated that 7 million Americans misused ADHD medications; and substantial numbers of teenagers and young adults show signs of addiction. “[A]bout 1.6 million teenagers and young adults had misused these stimulants during a 12-month period and that 75,000 showed signs of addiction.”

### **Should ADHD Medications Carry a Black Box Warning?**

In February of 2006 the FDA's Drug Safety and Risk Management advisory committee recommended that medications for ADHD carry a 'black box' warning (the Food and Drug Administration's strictest warning), because of the potential risks of heart damage and sudden death. Since nearly 3.3 million Americans age 19 and younger used an ADHD drug in 2005 (according to Medco Health Solutions Inc., a prescription drug benefit program manager), the panel decided a black box warning should be added because of the health concerns.

The unexpected vote came during a meeting when medical experts were being asked to determine “research approaches” that could be used to study whether ADHD drugs increase the risk of heart problems, according to an FDA description of the gathering. The potential heart-related concerns with ADHD medications include: stroke, hypertension, palpitations, arrhythmia and heart attacks. Of the 25 reported deaths, 19 were children. According to data presented to the advisory panel, a child on an ADHD drug increases his/her risk of sudden cardiac death by 1.5 to 2.5.

Members of the Safety and Risk Management advisory committee said the recommendation was driven as much by worries that ADHD drugs are being overused in the United States as by the possible side effects. About 10 percent of 10-year-old American boys are taking such medications. “On the surface, it is hard to believe,” said Curt Furberg, professor of public health sciences at North Carolina's Wake Forest University Medical School, who voted for the black-box warning. “What is also interesting is this condition is not really recognized in other countries -- you wonder what we are treating. I am sure there are patients who need these drugs, but it is not 10 percent of all 10-year-old boys.”

While diagnosis is most common in children, especially boys, physicians have recently started writing more prescriptions for adults. Cardiologist Steven Nissen of the Cleveland Clinic, who was one of the committee members who pushed for the warning label, said the growing use of ADHD drugs in adults is a serious concern because the risk of heart attack rises among adults older than 50.

While the FDA isn't bound by its advisory panels' recommendations, it usually does what the advisory panel recommends. However, many health professionals were concerned that the move to a black box warning was too severe given that the risk of a cardiac event is extremely low (less than one per million).

The FDA then asked a different advisory committee, the Pediatric Advisory Panel, to examine the cardiac event issue as well as reports that psychosis or mania can occur in some juvenile patients at normal doses of any ADHD drug. FDA investigators had discovered that some children with no identifiable risk factors suffered potentially traumatizing visions, although they cannot point to a definitive link, "the predominance of hallucinations involving insects, snakes and worms is striking." They noted a "complete absence" of similar reports in children treated with dummy pills during dozens of clinical trials of the drugs. In many children, the events ceased once they stopped taking the drugs — and resumed in some once they restarted. "That's unlikely to be due to random chance, suggesting some effect of the drugs," said Dr. Andrew Mosholder, of the FDA's division of drug risk evaluation.

The Pediatric Advisory Panel did not support the Safety and Risk Management Committee's recommendation for a black box warning, but did suggest that labeling information for ADHD medications be updated to warn of possible side effects including aggression, cardiovascular events, and psychiatric symptoms such as psychosis and mania. The minutes of the March 22, 2006 committee meeting referred to its recommendations as "a gathering of ideas for the agency to consider for labeling options."

As a result of the disagreement between the two FDA committees, it took the FDA several months to come to a decision about the conflicting labeling recommendations. As a matter of fact, it wasn't until February 21, 2007 that the FDA directed manufacturers of ADHD medications to notify patients about potential adverse cardiovascular and psychiatric events (implement the black box warning): "The U.S. Food and Drug Administration (FDA) today directed the manufacturers of all drug products approved for the treatment of Attention Deficit Hyperactivity Disorder (ADHD) to develop Patient Medication Guides to alert patients to

possible cardiovascular risks and risks of adverse psychiatric symptoms associated with the medicines, and to advise them of precautions that can be taken.” Patient Medication Guides are required handouts given when a medication is dispensed; and they contain FDA-approved patient information about the medication.

Anecdotal information on ADHD medications varies from describing how it enabled children to study more effectively to suggesting that it contributed to a successful suicide attempt or a chemical dependency problem. There is a tendency to over prescribe medication, so it’s not too surprising that ADHD medications are used in the attempted control of active 10 year old boys. But it seems that if we are not careful, we could be giving a new twist to an old proverb—Children should be neither seen nor heard—with devastating results.

In 1999, Psychiatrist Peter Breggin estimated that 4 to 5 million children in the U. S. receive psychostimulants each year. In a 1999 journal article, “Psychostimulants in the treatment of children diagnosed with ADHD: Risks and mechanism of action,” Breggin reviewed the adverse drug reactions associated with several well-known ADHD medications: dextroamphetamine (Dexedrine and Adderall) methamphetamine (Desoxyn and Gradumet), and Ritalin. He stated:

The drugs suppress spontaneous and social behaviors while promoting obsessive/compulsive or perseverative behaviors. These adverse drug effects make children more manageable in structured or controlled situations, especially those that lack sufficient adult supervision and attention. The effects are independent of any diagnosable disorder and occur in entirely normal animals and children.

Breggin went on to note that one of the gravest risks of these psychostimulants is that they will have the intended effect upon children—namely “suppress autonomous, spontaneous, social, playful behavior and bring about compliance, docility, and overly-focused obsessive and rote behavior.” The widespread use of stimulants enables adults to subdue and control children without improving their parenting or teaching; without addressing issues within the family structure and educational systems.

Similarly, in the mid 1800s, several decades before the widespread regulation of medications, the widespread use of opiate derivatives with children was a concern. Karl Marx even referred to the English working-class custom of "dosing children with opiates." A classic report on the English industrial system, *The Factory System Illustrated* (1842), by W.

Dodd, also noted how factory workers of the time used opiates—notably laudanum (opium mixed with alcohol and sometimes sweetened with sugar)—to quiet crying babies.

Godfrey's Cordial, a mixture of opium, molasses (for sweetening) and sassafras (for flavoring), was a popular remedy used as a “children’s painkiller.” An English chemist said it was “common practice” for mothers to give Godfrey's Cordial or laudanum to babies to in order to keep them quiet while the mother was at work. “It is not unknown for mothers to begin this practice with infants of a fortnight old commencing with half a teaspoon of Godfrey's or one or two drops of laudanum.”

In one family, four children met their deaths through taking this “infant cordial.” The following report, which appeared in the *Nottingham Journal* on December 20, 1845, illustrates the problem. An inquest into the death of Mira Newton, 17 weeks, revealed that since birth, the child had been given the “infants mixture to keep it quiet.” The final dose proved to be too strong and brought on a convulsion which led to Mira’s death. The inquest ruled it was a natural death, “accelerated by an overdose of a certain narcotic called Infants Mixture, or Godfrey's Cordial.” Although the medicine was administered by the mother, since she was ignorant of its effects, the mother was not held liable for her daughter’s death. Many babies died from similar causes without any inquiry or inquest held into their deaths.

It seems that we are repeating old mistakes in the age-old attempt to control our children. Breggin commented that:

The limited, questionable, and controversial benefit of stimulant drugs seems to pale beside their suppressive mental effects and many adverse reactions, including persistent brain dysfunction and potentially irreversible CNS damage. Pharmacological interventions in the brain to suppress spontaneous behavior and to promote obsessive ones is wrong in principle. Enough is already known about the lack of benefit and the negative impact of stimulants to stop prescribing them for “ADHD” or for the control of any symptoms or behaviors in children.

*For more information on this topic, see the following:*

“Attention-deficit hyperactivity disorder” at:

[http://en.wikipedia.org/wiki/Attention-deficit\\_hyperactivity\\_disorder](http://en.wikipedia.org/wiki/Attention-deficit_hyperactivity_disorder).

“‘Black Box’ ADHD Drug Warning Rejected” CBS news March 22, 2006:

[http://www.cbsnews.com/stories/2006/03/22/health/main1429683.shtml?CMP=OTC-RSSFeed&source=RSS&attr=Health\\_1429683?CMP=ILC-SearchStories](http://www.cbsnews.com/stories/2006/03/22/health/main1429683.shtml?CMP=OTC-RSSFeed&source=RSS&attr=Health_1429683?CMP=ILC-SearchStories).

“FDA Asks Attention-Deficit Hyperactivity Disorder (ADHD) Drug Manufacturers to Develop Patient Medication Guides.” See the following link for the FDA February 21, 2007 press release as well as the advisory committee transcripts:

<http://www.fda.gov/cder/drug/infopage/ADHD/default.html>

“Psychostimulants in the treatment of children diagnosed with ADHD: Risks and mechanism of action,” by Peter Breggin.

<http://www.breggin.com/Newstimulants.pdf>

“Severe Childhood ADHD May Predict Alcohol, Substance Use Problems in Teen Years:” <http://www.nih.gov/news/pr/aug2003/niaaa-17.html>.