ALLIANCE FOR HUMAN RESEARCH PROTECTION

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Testimony Submitted for the Record
by
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Hearing on the Utilization of Psychotropic Medication for Children in Foster Care

COMMITTEE ON WAYS AND MEANS
SUBCOMMITTEE ON INCOME SECURITY AND FAMILY SUPPORT

May 8, 2008

My name is Vera Hassner Sharav. I am a public advocate for human rights. I head the Alliance for Human Research Protection (AHRP), a not-for-profit national network of lay people and professionals dedicated to advancing responsible and ethical medical research and full disclosure of drug safety information. The AHRP board of directors includes physicians, a pediatrician, child psychiatrists, an ethicist, and professors of social work and education. The AHRP serves as a credible information resource, disseminating daily e-mails called "Infomails" that provide information about medical research ethics and drug safety issues. Of particular concern are vulnerable populations, especially children, the elderly, and people with disabilities.

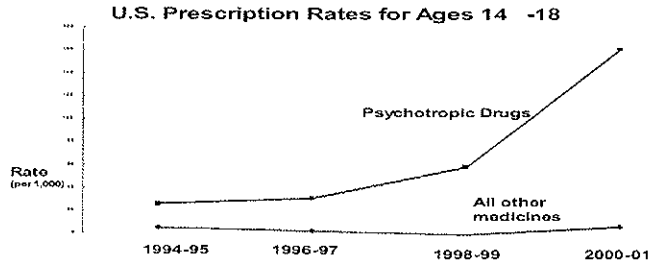
The AHRP Infomails have a wide following among patient advocacy organizations, members of the scientific community, public officials, the media, medical journal editors, and lawyers. The AHRP also maintains the website ahrp.org and a blog at ahrp.blogspot.com.

Our advocacy efforts have been undertaken on behalf of individuals victimized in unethical research experiments or harmed by concealed hazards of prescribed drugs. I have testified before national advisory panels—including the Institute of Medicine, the Office of Human Research Protection, and FDA Advisory Committees. I have served on the Children's Workgroup of the National Human Research Advisory Committee, and made presentations before the American Public Health Association, interns of the National Academy of Science, an ethics forum of the United States military, the New York Bar Association, and numerous

academic forums around the country. I have also authored articles appearing in Ethical Human Psychology and Psychiatry, Journal of Disability Policy Studies, and American Journal of Bioethics.

This committee is to be commended for holding this hearing to help bring to public attention that children are being irresponsibly prescribed drugs that induce debilitating life-shortening diseases.

Millions of American Children Are Prescribed Drugs Whose Toxic Hazards Are Undisclosed to Parents

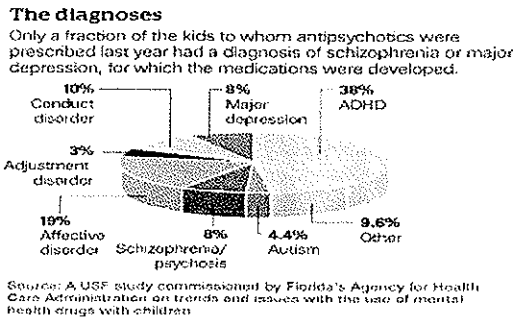


Brandeis study. Trends in the Use of Psychotropic Medications Among Adolescents, 1994 -2001. Psych Services, 2006

There is no medical explanation for the meteoric rise, beginning in 1994, in the rate of psychotropic drugs prescribed for American children.[1] Studies have found that 1 in 10 teenage boys visiting a doctor leaves with a psychotropic drug prescription—although 1 in 4 "did not have any associated mental health diagnosis." Another survey showed that child psychiatrists prescribe psychotropic drugs to 9 of 10 (91%)[2] children referred to them; **only 9% of children received psychotherapy.**

Worse, a 40-fold increase in prescriptions for the so-called 'atypical' antipsychotic drugs for children has been observed. They are prescribed indiscriminately for off-label behavioral issues—not psychosis for which they were approved for adults.[3]

Rampant Rx of Antipsychotics for US Children



A Vanderbilt University study reported that in 2001-2002, 2.5 million prescriptions were written in the United States for antipsychotics for children—and 53% of these prescriptions were for unapproved, "off-label" indications.[3] The drugs have been called "a chemical sledgehammer." As early as 1998, when children were exposed to Zyprexa in a UCLA study,[4] ALL children suffered adverse effects, none were helped, and the study was halted before 6 weeks.

Until now, the nature and scope of physiological harm and cognitive damage produced by antipsychotics has been denied or trivialized by psychiatry, the pharmaceutical industry, and the FDA. But evidence of profound harm is indisputable and leading scientists acknowledge that antipsychotics are the drugs with the most severely debilitating effects in the psychiatric arsenal. **Antipsychotic drugs disrupt normal functions of the central nervous system which controls all cognitive, emotional and neurological functions and most bodily systems** (including cardiovascular, endocrine, hormonal, pulmonary, gastrointestinal, urinary, and sexual.) As a result, a host of profound metabolic and bodily disturbances, some of which are fatal, may result.

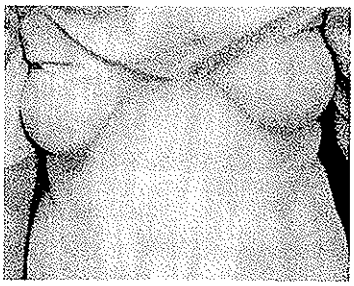
The authoritative government-sponsored CATIE study[5] found that adult patients receiving the antipsychotics Risperdal, Zyprexa, and Seroquel suffered severe adverse effects: 64%-82% dropped out. Risperdal induced "substantial increase in prolactin [hormone] levels" and **Zyprexa caused** "greater increases in weight and glucose and lipid metabolism than the other treatments...effects consistent with the potential development of the metabolic syndrome."

Adding insult to injury, these drugs' benefits have never been clinically demonstrated. They were approved without clear evidence of efficacy, only "proof in principle," that is, evidence of some effect over and above that of placebo. A 15-year follow-up study[6] confirms that even in adults for whom they were approved for psychosis, the drugs only help 5% to recover compared to a 40% recovery rate in those NOT on the drugs. Antipsychotics' labels now carry warnings about acute weight gain (>100 lbs), Type II diabetes, insulin resistance in children, hyperglycemia, liver / metabolic abnormalities, neuroleptic malignant syndrome, cardiovascular complications, stroke, early death in older frail patients...**However, parents are not told about those warnings.**

Pediatric data—from the Johnson & Johnson **Risperdal** trials and Eli Lilly **Zyprexa** trials—show that children and adolescents appear more likely than adults to suffer the most severe, life-threatening drug induced effects:[7] in one study, insulin resistance in all six children on **moderate** or **high** doses of antipsychotics, and in 3 of 5 children on **low** doses was observed. Dr. Mark Riddle, Director of Child Psychiatry at Johns Hopkins stated: "The

insulin resistance seen in these children was greater than what would be expected from weight gain alone, suggesting there is a factor distinct from excess weight that directly induces insulin resistance."

Though not life-threatening, a serious adverse effect—especially in boys—is the risk of developing breasts (gynecomastia). The picture below is of patient "J." Treated with Risperdal, at age 9.5 he developed breasts that required surgical removal at age 14.



A physician reported [8] that **"among 10 psychotic adolescents treated with Risperdal (risperidone) in our unit, we had 3 cases of gynecomastia in 3 male patients with risperidone-induced symptomatic hyperprolactinaemia in adolescents." The risk is not disclosed to parents—evidence comes from plaintiff lawyers.**

Antipsychotic drugs diminish the quality of children's lives, possibly forever. Black Box labels warn about strokes and death in the elderly, but there is no evidence that the same risks of death don't apply in children. The drugs have not been tested long enough in children to detect uncommon but potentially lethal effects.

Two experiments testing Risperdal in children show the range of alarming adverse effects suffered by the children. The reports were published in the *New England Journal of Medicine* (2002)[9] and in *Pediatrics* (2004).[10]

% of Risperdal Adverse Events Over 8 Weeks: Children Aged 5-17 Yrs

Adverse Event	*Risperdal (n= 49)*	*Placebo (n=52)*
Fatigue	59%	27%
Drowsiness	49%	12%
Constipation	29%	12%
Skin irritation	22%	14%
Drooling	27%	6%
Dyskinesia (involuntary movements)	12%	6%
Tremor	14%	2%
Tachycardia	12%	2%
Muscle rigidity	10%	2%
Respiratory infection	10%	4%
Sore throat	10%	2%

From: McCraken et al. (2002). *NEJM*, 347:314-321.

% of Risperdal Adverse Events Over 8 Weeks: Children Aged 5-12 Yrs

Adverse Event	*Risperdal (n= 40)*	*Placebo (n=39)*
Somnolence	72.5	7.7
Abdominal pain	20	7.7
Constipation	12.5	2.6
Apathy	12.5	0
Tachycardia	12.5	0
Flu-like symptoms	10	5.1
Fatigue	10	2.6
Weight gain	10	2.6
Tremor	10	0
Involuntary movements	27.5%	12.8

From: Shea et al. (2004). *Pediatrics*, 114:e634-e641.

Responsible voices are raising alarm bells: Dr. Steven Hyman, a neuroscientist and Former NIMH Director: *"We have to realize that we are risking treating children who could turn into obese diabetics with involuntary movements."* **Dr. John March** Chief of Child Psychiatry, Duke University: *"We are using these medications and don't know how they work, if they work, or at what cost.* ***It amounts to a giant experiment with the lives of America's children****... with no data to know whether these drugs are effective or safe over the short term, much less the long term."*

Despite antipsychotics' demonstrably **poor clinical performance**, despite "staggering" adverse effects, that are even worse in children and adolescents, off-label prescriptions for US children / adolescents surged by 82% from 2001 to 2006 (Medco).[11] A 2006 Columbia University study[12] confirms that psychiatrists and other prescribing physicians are disregarding the staggering risks for children. Between 1994-2004, the diagnosis of bipolar disorder in adults increased twofold. By comparison, in children, which had virtually never received such a diagnosis, it increased 40-fold (two thirds of children labeled as "bipolar" are boys). Treatment for such an alleged condition in children is virtually always with antipsychotic or anticonvulsant drugs, usually in combination. "One in five psychiatric visits by young people includes a prescription for antipsychotics—90% were prescribed by psychiatrists." The study's principal investigator, Dr. Mark Olfson, stated: "There is an urgent need to evaluate the drugs' safety and effectiveness."[12]

This is not quite so. The jury is in already, and the drugs are neither safe nor effective. As mentioned, most prescriptions for antipsychotics are for off-label indications, such as ADHD. Yet, a 1998 UCLA Zyprexa trial in children with ADHD had to be suspended because ALL children suffered adverse effects and NO child was helped.[4] If the drugs are so helpful and the risk-to-benefit ratio is acceptable to parents, where are the independent, controlled

studies showing such clear benefits? There are none. Aside from the high profits these drugs bring, their drugs' widespread use among troubled children is, as Texas Comptroller **Carole Keaton Strayhorn**[13] declared: "... a **chemical sledgehammer** that makes children easier to manage."

According to Dr. **Joseph Woolston,** Chief of Child Psychiatry at Yale University, *"Tens of thousands of kids are on random combinations of psychoactive drugs...**We're using them as guinea pigs, and not even keeping track of them."*** Those at greatest risk of such irresponsible prescribing are children in foster care and those covered by Medicaid.[13]

In 2006, *USA Today* reported that a MEDCO analysis of FDA's voluntary adverse reporting system, MedWatch—which had been mandated by Congress—revealed that 45 children's death reports between 2000-2004 suspected a link to antipsychotics. There were another 41 reports of neuroleptic malignant syndrome—which, if unrecognized or untreated, poses a fatal risk within 24 hours. There were more than 1,328 reports of antipsychotic-linked serious side effects in children. Reports to MedWatch represent a mere fraction—estimated at between 1% and 10%—of the actual adverse effects observed by physicians. Dr. Laughren's response, reported in *USA Today*,[14] speaks for itself: "we haven't been alerted to any particular or unusual concern...The effects (in kids) are similar to what we're seeing in adults."

Despite all these known risks and concerned voices, and the lack of effectiveness of the drugs in adults and children, the FDA approved Risperdal for use in autistic children in October 2006, and Abilify for mania in teens in November 2007 based on a 6-week study. Perhaps, as alarming as the approval of the drug for children, is the process that led to the approval. FDA failed to impose any restrictions on the use of Risperdal for irritability in autistic children—and they conducted their deliberations in secret.

FDA issued the Risperdal marketing license after the company withdrew its application in the UK on June 8, 2006,[15] following the determination by UK Medicines Authority (MHRA) that "safety problems" necessitate strengthened restrictions on conditional approval for: "the short-term treatment of severe aggression and violence whether directed towards self or others in autistic children where available nonpharmacological methods have first been tried and failed." The MHRA further specified monitoring requirements "under black triangle status" and submission of "a full risk management plan with defined milestones for data... which would include a registry of children on risperidone so that the effects of longer term risperidone therapy could be adequately monitored." Shouldn't concerns about the safety of Risperdal andother newer antipsychotics for children have compelled the FDA to be especially conservative and

cautious in the transparency of their proceedings?

On April 29, 2007, Dr. Thomas Laughren overruled FDA's team of safety officers and issued an approvable letter to Eli Lilly for pediatric use of Zyprexa (olanzapine) despite serious concerns about the integrity of the data obtained in Russia.[16] Encouraged by the approval of Risperdal for children, other competitors filed similar applications. On June 9, 2007, Bristol-Myers announced that FDA granted priority review for its application to market Abilify (aripiprazole) for teenagers; on June 21, 2007 FDA issued an approvable letter to Johnson & Johnson to expand the use of Risperdal to teens. On October 20, 2006, the FDA approved AstraZeneca's application for the use of Seroquel® (quietiapine) in the treatment of major depressive episodes associated with bipolar disorder[17]—**despite the fact that a major government review of off-label prescribing of antipsychotics found no evidence demonstrating clinical efficacy for bipolar depression.**[18] Strangely, at the time that the FDA was issuing approvals for use of antipsychotic drugs in children, officials deferred the pediatric study requirements for Abilify until December 2011.

Were these approvals science-based decisions or marketing decisions? Clearly, American children's physical and mental health is being undermined by toxic drugs prescribed by child psychiatrists and other physicians under the undue influence of the pharmaceutical industry.

AHRP's June 27, 2007 letter to FDA Commissioner, Dr. Andrew von Eschenbach, informed him that an AHRP investigation uncovered an apparent conflict of interest by the official in charge of FDA's psychiatric drug approval division. The letter, posted on the AHRP blog, http://www.thejabberwock.org/blog/2/20070627ahrpfda.pdf documents evidence that raises questions about whether Dr. Thomas Laughren, FDA's highest ranking official in charge of psychiatric drug products, has a conflict of interest contributing to the problem of children's exposure to antipsychotics. Dr. Laughren's close ties with industry and his name penned to industry-sponsored consensus conference reports (ghost-written, we should add) may explain the recent inexplicable surge of FDA administrative approvals for the expanded use of toxic antipsychotic drugs for children.

These approvals were determined after secret deliberations—without disclosure of scientific data, without an advisory panel or open public discussion. No credible evidence of a clinical benefit for any childhood "condition" has ever been presented by independent, non-industry generated studies to offset the well-documented evidence of the debilitating and disabling effects produced by these drugs.

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