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FYI

The FDA has just announced New Warnings acknowledging an increased risk in suicidal thinking, behavior in Young Adults who take antidepressants.

<http://www.fda.gov/bbs/topics/NEWS/2007/NEW01624.html>

The new warnings extend the Black Box warnings about these drugs' hazardous effects in children and adolescents to adults under 25.

The FDA claims it is guided by scientific evidence. Why then, has the FDA ignored the evidence in its possession?

The suicide risk associated with Prozac was first recognized and documented by the German Medicine Authority, in 1984. [1]

In 1985 FDA's safety review officer listed 52 cases of "catastrophic and serious events" in Eli Lilly's Prozac trials--some had not been reported by the company. (<http://www.baumhedlundlaw.com/08.pdf>)

In 1990 Drs. Martin Teicher and Jonathan Cole, reported in the American Journal of Psychiatry that "persistent, obsessive, and violent suicidal thoughts emerged in a small minority of patients treated with fluoxetine."

[2]

(<http://www.baumhedlundlaw.com/10.pdf>).

A 1990 FDA internal memorandum indicates that the FDA believed the public controversy that had erupted concerning the potential for antidepressants to increase the risk of suicide in adults was not "a real issue, but rather, a public relations problem." [3]

In 1991 the FDA convened an advisory committee hearing, declaring "No evidence." FDA dismissed the testimony of victim families and took absolutely no action.

The new warnings follow the recommendations of FDA's advisory committee (November 17, 2006).

The FDA's clinical review of the suicidality data in adults, submitted to the psychopharmacological advisory committee showed the Relative Risk (RR) of Suicidal Behavior to be:

Age <25: RR = 2.30 (Confidence Interval, 1.04 - 5.09)

Age 45 - 54: RR = 2.29 (CI, 0.73 - 7.14)

Age 45 - 64: RR = 1.75 (CI, 0.68 - 4.48)

See: <http://www.fda.gov/ohrms/dockets/ac/06/briefing/2006-4272b1-index.htm>

See also:

http://www.fda.gov/ohrms/dockets/ac/06/slides/2006-4272OPH1-11-sharav_files/frame.htm

After more than two decades of consistent evidence from clinical trials and MedWatch reports showing a suicidal risk for adults and children taking Prozac and the other SSRI antidepressants, the FDA position continues to limit its acknowledgment of the documented risk :

"Attempts and suicides in kids and young adults"

Ever so gradually, after thousands of preventable deaths, the FDA is inching forward from issuing no warnings, to issuing precautions, to issuing warnings for children / adolescents (2005) --only AFTER being interrogated in congressional hearings.

In 2007, the FDA is coming around to adding warnings for Young Adults, while still disregarding the evidence that consumers aged 45 -54 have the same relative risk for drug-induced suicidal behavior as do young adults and adolescents. Indeed, an increased relative risk extends to age 64.

One of the keen scientists who supports the AHRP mission of promoting full disclosure about drug safety issues to the public, forwarded the following apt Steve Martin routine:

"I used to smoke marijuana. But I'll tell you something: I would only smoke it in the late evening..... Oh, occasionally the early evening, but usually the late evening - or the mid-evening..... Just the early evening, midevening and late evening. Occasionally, early afternoon, early midafternoon, or perhaps the late-midafternoon. Oh, sometimes the early-mid-late-early morning. . . . But never at dusk. I would never do that."

Antidepressants are not designed to differentiate between ages 15 and 25 or 45. The drugs have consistently been shown to trigger suicidal and homicidal behavior--even in non-depressed people since the early trials in Germany. So, FDA's efforts to obfuscate and deny the scientific evidence might be funny if the agency's failure to take action hadn't resulted in thousands of preventable human tragedies.

FDA position: 1987--1997: "No evidence" "no evidence" "no evidence"

1997: "the possibility of suicide is inherent in depression"

"Suicidal thinking but not attempts, and just in kids"

"Attempts, just in kids, but no suicides"

"Attempts in kids, but not adults"

"Attempts and suicides in kids and young adults, but not older adults."

Never in middle age adults.

Why does the FDA have to be dragged to issue warnings only when Congress is about to deliberate about drug safety?

Below, an article in The News Journal (Delaware) attempts to provide a balanced perspective to the antidepressant drug safety / efficacy debate. Still much of the information is filtered through industry channels and passed on as if it were validated.

Those who are quoted favoring the use of these drugs in children--despite documented evidence of increased risks of harm--are not disinterested, objective observers. Most are financially dependent on drug manufactures.

For example, at the center of the article is Kelli Burris, the mother of a 16 year old who is taking multiple psychotropic drugs--an unapproved drug cocktail. Ms. Burris works for the National Alliance for Mental Illness (NAMI) and is active in the Child and Adolescent Bipolar Foundation (CAB).

NAMI received \$544,500 from Eli Lilly during the first quarter of 2007. "Walk for the Mind of America" which is featured at the end of the article is funded by Eli Lilly as well.

https://www.lillygrantoffice.com/docs/q1_registry_report.pdf

CAB is funded by the major psychotropic drug manufacturers, including Eli Lilly, Pfizer, GlaxoSmithKline, Johnson & Johnson, etc.

http://www.bpkids.org/site/PageServer?pagename=ppl_organizational_donors

NAMI and CAB promote the unapproved prescribing of powerful psychotropic drugs for children--even in drug cocktails which have NEVER been tested for safety or efficacy. The hazardous effects of such off-label prescribing are documented in hospital emergency admissions.

Responsible clinicians hotly criticize such prescribing practices--but not those who are financially dependent on drug companies.

References:

1. May 25, 1984: "During the treatment with the preparation [fluoxetine] 16 suicide attempts were made, 2 of these with success. As patients with a risk of suicide were excluded from the studies, it is probable that this high proportion can be attributed to an action of the preparation in the sence (sic) of an deterioration of the clinical condition, which reached its lowest point." Internal memorandum from Eli Lilly regarding the company's efforts to obtain a marketing license for Prozac in Germany: See:

<http://www.baumhedlundlaw.com/01.pdf>

2. Martin H. Teicher, M.D., Ph.D., Carol Glod, R.N., M.S.C.S., and Jonathan

O. Cole, M.D. Emergence of Intense Suicidal Preoccupation During Fluoxetine Treatment, Am J Psychiatry 1990; 147:207-210.

3. FDA official, Dr. Martin Brecher, indicated to GSK that the FDA "does not think it is an issue" but rather, "a public relations issue" "but it needs to be addressed." (<http://www.baumhedlundlaw.com/12.pdf>)

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<http://www.delawareonline.com/apps/pbcs.dll/article?AID=/20070501/HEALTH/705010354/-1/NEWS01>

The News Journal

The debate over drugs, teen and depression

Concerns abound over antidepressants' impact on suicidal feelings in young people, but some experts say they're the best option

By HIRAN RATNAYAKE,

Tuesday, May 1, 2007

Jacqueline Lewis, 16, and her mother, Kelli Burris, play a board game. Jacqueline suffers from bipolar disorder and depression. Some critics contend that antidepressants can increase suicidal thoughts among teenagers, but Burris said they saved her daughter's life. Lewis' medications include the antidepressant Luvox. A recent study in the Journal of the American Medical Association found that prescribing antidepressants to young people with mood disorders outweighs the risks.

Dr. Saleem Khan, chief of psychiatry at Delaware Guidance Services, says antidepressants can help youth more than they have the potential to hurt. On her MySpace page, 16-year-old Jacqueline Lewis reveals a very personal detail:

"for those of you who don't know me ii am Bipolar -- a mood disorder."

She also suffers from depression. And at times, she's even told her mother she has wanted to die. "I've wanted to escape this world," said Lewis, a sophomore at Middletown High School. "I've thought about ending my life."

These days, Lewis is feeling pretty good, though she still deals with occasional highs and lows. She and her mom credit the prescription drug Luvox. She has taken Luvox regularly for the past decade despite the Food and Drug Administration's decision in 2004 to give the antidepressant the black box warning, meaning it may cause serious adverse effects such as

increased suicidal thoughts. Lewis' mom, Kelli Burris, said keeping her daughter on the medication has been the right choice, and she worries that the FDA's warning has deterred other parents from putting their kids on antidepressants that could benefit them. "I don't think Jacqueline would be alive today without the medications," she said.

She has company. Researchers recently analyzed data on 5,310 children and teens from 27 studies in which children were asked questions about their mood and feelings. They found that for every 100 young patients treated with antidepressants, only about one child experienced worsening suicidal feelings during the first few weeks of treatment. (The FDA, by contrast, found three years ago that the added risk affected about two in 100 kids, prompting the agency to add the black box warning.)

The researchers concluded, in the latest issue of the Journal of the American Medical Association, that the benefits of prescribing antidepressants for young patients trumped the risks, although the drugs did better in treating anxiety than what they're designed to treat -- depression.

Still, the debate on whether to medicate kids with mental illness continues. Some people believe doctors and parents -- society, in general -- are too quick to use pills to address problems and bypass other methods, such as therapy. "We have been overwhelmed with messages that say any little problem can be fixed with a pill," said Vera Sharav, president of the Alliance for Human Research Protection, an advocacy group.

### Types of drugs

Antidepressant drugs known as SSRIs, or selective serotonin reuptake inhibitors, became the first-line therapy for depression after the FDA's approval of Prozac in 1987. Zoloft followed in 1991 and Paxil in 1992. By the mid-1990s, Prozac was one of the most commonly prescribed medicines internationally, with sales totaling more than \$2.5 billion.

Among antidepressants, only Prozac is approved to treat depression in young patients. But others have been used off-label by psychiatrists for years to treat children and teens.

In early 2004, the FDA held a hearing on the elevated risk of suicidal thoughts among young patients taking SSRIs. In October of that year, a black box warning was ordered on all antidepressant medications stating that the drugs may cause an increased risk of suicidal thoughts in children and adolescents. In the six months after the hearing but before the warning was ordered, antidepressant prescriptions by pediatricians dropped by about 10 percent, according to the American Academy of Child and Adolescent

Psychiatry.

Michael Houston, a child psychiatrist from Maryland and member of the academy, said pediatricians had been pre-scribing antidepressants in an attempt to treat depression in children when therapy wasn't available. "You had this situation where pediatricians and family care doctors were turning to [antidepressants] to help these kids out," Houston said. "But afterward they were responding to the concerns about the side effects."

Some parents made the leap that antidepressant drugs may increase the suicide rate among young people who use them, when in fact the black box warning was added because the drugs may increase thoughts of suicide among those taking them -- and only during the first few weeks of treatment, said Dr. Saleem Khan, chief of psychiatry at Delaware Guidance Services for Children & Youth, a provider of outpatient mental health services for children and their families. These parents may have thought that since their child was already depressed, the antidepressants would put them more at risk for committing suicide, said Khan, also clinical director for child and adolescent services for Rockford Center in Newark.

But he said antidepressants have been shown to help, and he believes the benefits of prescribing the drugs outweigh the risks, especially when children don't respond to other treatment options. Parents shouldn't just ask their child's pediatrician to prescribe antidepressants, though, and children who do end up going on the drugs should be monitored intensely during the first few weeks of their trial, he said.

"Sometimes we may agree that the best thing to do is to wait a while," Khan said. "Other times I'll tell the parents to definitely seriously consider the trial of an antidepressant, especially if they're suicidal."

Behavioral changes

Not all people have the same experience as Jacqueline Lewis and her mom. Kathleen Osburn's son, Graem Caliendo, suffered from depression as a child. He would be all smiles one minute and crying uncontrollably the next -- with no explanation. So she decided to put Caliendo, 10 at the time, on the antidepressant Wellbutrin. "It's very painful to see your child that way," said Osburn, a Wilmington native who now lives in West Chester, Pa. "I thought, 'Let's give it a try.' "

Caliendo did come out of the depression, but he became aggressive and started fighting with his classmates. Osburn took him off the drug after just three months. A decade later, he remains on mood stabilizers instead of antidepressants, which seems to have worked much better for him. Caliendo, now 20 and living in Pittsburgh, said he vaguely remembers the schoolyard fisticuffs. "I think it has everything to do with my brain

chemistry, and it was probably affected by the stuff I was on," he said. "But I don't know if [the antidepressants] are actually causing people to commit suicide or not."

Osburn said she supports the FDA's black box warning of possible serious side effects in young people. "I know the FDA warning is scary and frightening, but I think it makes parents stop and think about what they're doing," said Osburn, who does not regret putting her son on the Wellbutrin trial but is glad she made the decision to take him off it so quickly.

Sharav of the Alliance for Human Research Protection wants the government to severely restrict antidepressant use in young patients. She is familiar with the latest JAMA study that concludes the benefits of antidepressant use outweigh the risks. But she said the emphasis should be on the fact that antidepressant drugs weren't highly successful in treating depression.

The drugs worked best in treating anxiety, moderately well in treating obsessive-compulsive disorders and less well, but still effectively, in treating depression. "They trigger very adverse side effects, like aggression and hostility," she said. "In other words, 'homicidal behavior.'"

It has been reported that Eric Harris, one of the two perpetrators in the Columbine High School massacre, was on Luvox at the time he carried out the killings and then committed suicide. "The suicides that occur with people on these drugs are not like the old drugs," Sharav said. "These suicides are violent."

'Like we turned a light switch on' The choice to medicate children with antidepressants, however, may be driven in part by cost.

Houston, who researches insurance reimbursement issues for the American Academy of Child and Adolescent Psychiatry, said a month's supply of antidepressant pills could cost \$100 without insurance, whereas a month of weekly therapy sessions could run \$500 to \$800 without insurance. Insurance typically covers only 20 visits a year. "There's a pressure toward putting children on a medication because it's the cheaper treatment in the long run," he said.

Dr. Peter Zorach, a pediatric and adolescent psychiatrist in Wilmington, said therapy works but often takes a long period of time. "It's reasonable to do therapy alone," he said. "[But] if it doesn't work, you may have to try medicine."

Jacqueline Lewis, who is on three medications in addition to Luvox, still sees a psychiatrist each month.

"She couldn't eat at a restaurant, she couldn't wear pajamas, everything bothered her," said Kelli Burris, her mother. "When she was put on the correct medications it was like we turned a light switch on and we had a different child."

Last July, Burris began working for the National Alliance on Mental Illness in Delaware, which many parents turn to when they are contemplating antidepressants for their kids. The national organization's biggest contributors are drug manufacturers.

Rita Marocco, executive director of NAMI-DE, said parents are aware of the suicide risk and typically struggle with whether to put their children on antidepressants. But the benefits surpass the risks, she said, and therefore it's a risk worth taking. "We don't know the long-term effects of any drug," she said. "But we do know the effects of suicide."

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#### WARNING SIGNS OF SUICIDE

Suicide is the third-leading cause of death for 15- to 24-year-olds, surpassed only by accidents and homicide, according to the Centers for Disease Control and Prevention.

Suicide among teens often occurs following a stressful life event, such as a perceived failure at school, a breakup with a boyfriend or girlfriend, the death of a loved one, a divorce or a major family conflict.

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