

Doctors Fail to Recognize Life-Threatening Serotonin Syndrome

In addition to recent reports that the drugs work no better than sugar pills, the latest warnings added to the long list of adverse events linked to selective serotonin reuptake inhibitor antidepressants have focused on birth defects, suicide risks and violence.

However, the massive over-prescribing of SSRIs, including Prozac, Paxil, Zoloft, Celexa and Lexapro in combination with many other drugs now has medical experts scrambling to educate doctors about a life-threatening condition known as "serotonin syndrome."

According to the report, "A Mix of Medicines That Can Be Lethal," by Jane Brody, in the February 27, 2007 New York Times, "with the enormous rise in the use of serotonin-enhancing antidepressants, often taken in combination with other drugs that also raise serotonin levels, emergency medicine specialists are trying to educate doctors and patients about this not-so-rare and potentially life-threatening disorder."

According to the Times, patients at particular risk, some experts say, are those taking a combination of antidepressants and antipsychotic drugs prescribed to treat resistant depression.

Ms Brody notes that in the March 2005 New England Journal of Medicine, two specialists, Dr Edward Boyer of the University of Massachusetts Medical School and Dr Michael Shannon of Children's Hospital Boston, found that more than 85% of doctors were "unaware of the serotonin syndrome as a clinical diagnosis."

In a report based on calls made to poison control centers in the US in 2002, the doctors found 7,349 cases of serotonin toxicity and a total of 93 deaths. In 2004, the Toxic Exposure Surveillance System identified 48,204 exposures to SSRIs that resulted in moderate or major outcomes in 8,187 patients and death in 103 patients, according to the September 2005 American Journal of Emergency Medicine.

In 2005, the last year for which statistics are available, a total of 118 deaths were reported, according to the New York Times.

The true incidence of serotonin syndrome, experts say, may be under-reported in these figures because the syndrome may be wrongly attributed to another cause, mild cases may be dismissed or medical professionals may not suspect the condition.

Studies have shown that when an expectant mother takes an SSRI, her system is flooded with extra serotonin, which then passes across the placenta into the womb, soaking the developing fetus in serotonin, according to Houston Attorney Robert Kwok.

"It is this prolonged and unanticipated exposure to serotonin," he says, "that our experts believe leads to the baby's birth defects."

Studies indicate," he explains, "that mothers who take an SSRI during pregnancy have 1.5 to 2 times the risk of giving birth to a baby with a heart defect such as an atrial septal defect or ventricular septal defect, and are 6 times more likely to give birth to a baby with a severe and life-threatening lung disorder known as persistent pulmonary hypertension (PPHN).

And the cases of birth defects are on the rise. "Our group has over 100 SSRI baby birth defect cases in medical review," Mr Kwok states, "with most babies bearing strikingly similar heart and lung defects."

Mr Kwok is representing the family of Chase Steele, a baby born with severe heart defects after his mother took an SSRI during her pregnancy and the family of Gavin Shore, an infant also with severe heart defects to a mother who took the SSRI Celexa during her pregnancy.

"You would think by now," Mr Kwok says, "that the FDA would ban SSRIs for children, since the same logic applies to developing adolescents and developing babies in the womb during pregnancy."

Serotonergic receptors are found throughout the central nervous system and are involved in the regulation of the sleep-wake cycle, behavior, appetite, temperature and muscle tone, and serotonin neurotransmission is involved with the regulation of gastrointestinal motility and vascular tone. Serotonin syndrome results from excessive stimulation or agonism at postsynaptic serotonin receptors.

According to the FDA, symptoms of the syndrome may include restlessness, hallucinations, loss of coordination, fast heart beat, rapid changes in

blood pressure, increased body temperature, overactive reflexes, nausea, vomiting and diarrhea.

The patients often have changes in mental status, including agitation, hypervigilance and pressured speech, and in severe cases, may present with profound hypertension and tachycardia, and proceed rapidly to shock.

In severe cases, patients may exhibit delirium, seizures, muscular rigidity and hypertonicity. A core temperature may exceed 40°C (104 F), and may be accompanied by metabolic acidosis, rhabdomyolysis, renal failure and disseminated intravascular coagulation.

Experts say the most important information for doctors to know when dealing with a possible case of serotonin syndrome is what drugs have been ingested, because in addition to SSRIs, there are other classes of drugs with different mechanisms that can also increase serotonin levels to differing degrees.

A greater awareness of the combinations that trigger the syndrome could lead to prevention, but a diagnostic challenge exists due to the fact that the list not only includes prescription drugs, but also over-the-counter medications and herbal supplements. The following are some of the products known to be associated with serotonin syndrome:

- Monoamine oxidase inhibitors (MAOIs)
- Tricyclic antidepressants (TCAs)
- Selective serotonin reuptake inhibitors (Zoloft, Prozac, Paxil, Lexapro, Celexa)
- Venlafaxine (Effexor)
- Trazodone (Desyrel)
- Nefazodone (Serzone)
- Meperidine (Demerol)
- Dextromethorphan (Cold Remedies)
- Chlorpheniramine
- Sumatriptan (Imitrex)
- Atypical antipsychotic (Zyprexa, Risperdal, Seroquel)
- L-dopa
- Meridia
- Lithium
- Valproic acid (Depakene)
- Linezolid (Zyvox)
- St John's Wort
- Ginkgo Biloba

Many experts blame the rise in cases of serotonin syndrome on the fact that so many different drugs are being prescribed to patients at the same time in combinations, or "drug cocktails," which have never been approved as safe and effective by the FDA for any use and without considering the over-the-counter medications that patients may be taking.

The syndrome has become more prevalent in children as the off-label use of drug cocktails with children has increased. Some experts suspect serotonin syndrome in the death of 4-year-old, Rebecca Riley in Massachusetts, on December 13, 2006.

Critics say the Riley case highlights the need to put an end to the rampant off-label prescribing of adult psychiatric drugs to children. "The general public is unaware that almost no psychiatric drugs have ever truly been tested for children," according to David Oaks, director of MindFreedom, an international human rights organization.

"All psychiatric drugging of children," he says, "is essentially 'off label' in the sense that doctors have an enormous range of discretion when prescribing psychiatric drugs to young people."

"It's time for society to get hands-on with the mental health system," Mr Oaks warns, "and rein in the immense tyrannical power that doctors now have."

The State Police investigator's report in this case said psychiatrist Dr Kayoko Kifuji, at the Tufts-New England Medical Center, prescribed 3

medications for Rebecca: 750 milligrams a day of Depakote; 200 milligrams a day of Seroquel; and .35 milligrams a day of clonidine.

Rebecca was given Seroquel, for bipolar disorder, a drug only approved to treat adults with schizophrenia or bipolar, Clonidine, for attention deficit disorder, a drug approved only to treat adults with high blood pressure, and Depakote, an anti-convulsant drug approved to treat epilepsy in adults.

She was kept on this 3-drug cocktail since she was 2 and a-half-years-old, until she was found dead on the floor of her parent's home on December 13, 2006. At the time of her death, there were also over-the-counter cold medications in her system including Children's Tylenol Cough and Runny Nose, which contain acetaminophen, dextromethorphan and chlorpheniramine.

According to a report by investigators, Rebecca's teachers and a school nurse repeatedly complained about the child's extreme lethargy and how she seemed better when the drugs wore off, and the nurse also pointed out that Rebecca did not exhibit the kind of behavior that might justify prescribing these types of drugs.

A therapist who treated the children also told investigators she was concerned about the medications prescribed to Rebecca because she never noticed symptoms of attention deficit or bipolar disorder.

A state trooper's affidavit said a Walgreen's pharmacy filled a number of clonidine prescriptions for the Riley's when they should have had an ample supply and that several times, Dr Kifuji approved extra pills because Carolyn Riley said she had run out or lost her supply.

Carolyn Riley told investigators that Dr Kifuji had authorized the extra doses to help Rebecca get to sleep, the affidavit said. The trooper also reported that Dr Kifuji received calls from a therapist and a nurse at Elden Johnson Early Childhood Center, where Rebecca was a student, saying they were concerned about her medication.

The affidavit shows that no testing was conducted on Rebecca in making the diagnosis of attention deficit or bipolar disorder and that Dr Kifuji said she diagnosed Rebecca based on the parents' statements and "brief visits" in her office as frequently as twice a month and as seldom as once every two months.

In July 2006, a social worker treating Rebecca filed a complaint with the agency reporting that Carolyn Riley was "neglecting her children" and "appeared heavily drugged and unable to respond" on one of her visits to the family home.

The social worker said that during one visit, Carolyn told her that urine on the floor was from when Rebecca had taken a nap on the floor, according to an affidavit from investigators, and the social worker said she had to tell Carolyn to clean the floor.

When checking out the social worker's complaint, the DSS Commissioner said all the doctors and a psychiatric hospital caring for one of the children in July 2006 said the medications were appropriate and there was no one else to consult, so the department did not substantiate the complaint.

The medical examiner's office determined that Rebecca died from "intoxication due to the combined effects" of the drugs clonidine, Depakote, dextromethorphan, and chlorpheniramine, the district attorney's office said in a statement.

The official autopsy report states that Rebecca died of the "combined effects" of the drugs and that her lungs and heart were damaged by "prolonged abuse of these prescription drugs, rather than one incident."

Those findings have some experts wondering whether the medical examiner may be a member of the 85% of doctors identified by the New England Journal of Medicine study who are unaware of the serotonin syndrome as a clinical diagnosis.

The statement released by the DA states, "This occurred as a result of the intentional overdose of Rebecca with clonidine," and the manner of death "was determined to be homicide."

Rebecca's parents have both been charged with murdering their daughter.

However, psychiatrist Dr Grace Jackson, a leading authority on psychotropic drugs, takes issue with the claim of the manner of death being homicide.

"I'd put my money on serotonin syndrome as the cause of death," she says, "a potentially lethal condition of serotonin excess, leading to signs and

symptoms which include autonomic instability, heart dysrhythmias (sudden death), hyperthermia (high fever), changes in mental status (including possible coma), hyperreflexia, and myoclonus."

"In this case," Dr Jackson says, "the primary culprits were dextromethorphan and chlorpheniramine, an antihistamine which also boosts serotonin levels."

"It is probably quite likely," she explains, "that the family had not been warned by any doctor or pharmacist that this combination of medications could cause death — particularly, in a toddler."

"It is also possible," she adds, "that the psychiatrist did not realize that the family was administering dextromethorphan to the child --- it might have been given from an over-the-counter cough remedy by unsuspecting parents."

Dr Jackson also notes that Depakote has been shown to increase levels of serotonin in many brain regions, "hence," she says, "it was factor #3 in the serotonin syndrome which presumably killed this child."

"This toddler," she explains, "may have been receiving tiny doses of the medications prescribed, but that did not protect her from serotonin syndrome."

Reports by investigators, based on interviews of relatives in the home who observed Rebecca in the days before she died, describe symptoms typical of serotonin syndrome. They said she became restless, disorientated, incoherent, would not respond to her name and that she appeared dazed and "out of it."

She was lethargic at school and at home, and a neighbor described her as zombie-like, according to interviews in an affidavit filed in Plymouth District Court.

The day before she died, Rebecca developed a fever and was coughing uncontrollably, so her parents went to Wal-Mart to buy cold and flu medicine. While at Wal-Mart, Rebecca began to vomit, so Carolyn Riley purchased Pedialyte and a plastic bowl for Rebecca to vomit in during the ride home, and she reportedly vomited about 5 times over the course of that day.

Rebecca's grandmother told reporters that the doctor never told the parents not to give her the over-the-counter cold medications now listed as contributing to her death because of the prescription drugs she was on.

Dr Jackson suspects that Rebecca "like so many patients" was the unwitting victim of "Evidence Based Psychiatry," which means drug, drug, and more drug, because "somebody, somewhere, published a study that showed a three year old responded to five or six or seven drugs in combination," she states.

Dr Jackson is the author of, "Rethinking Psychiatric Drugs: A Guide for Informed Consent," a book that provides a critical appraisal of 3 classes of psychiatric drugs that an estimated 20% of Americans consume on a regular basis, including antidepressants, antipsychotics and stimulants.

According to Harvard Instructor Dr John Abramson, author of, "Overdosed America," this "gruesome story" seems to have two separate and distinct components. "First," he says, "is the question of whether or not the child was being given medication as it was prescribed."

"And the second," he notes, "is the question of why such medicines were prescribed for such a young child."

Dr Abraham points out that there has been a progressive medicalization of other than desirable behaviors in children. "We have seen this in the enormous proliferation of stimulant medication use," he notes, "far out of proportion to use in other countries."

Now, he says, the diagnosis of bipolar disorder in children is rising in parallel, and clearly, it is the drug industry driving this medicalization to sell more products.

In what can only be described as assembly-line customer recruitment, Rebecca's psychiatrist, Dr Kifuji, also prescribed the same powerful drug cocktail to Rebecca's older brother and sister when they were diagnosed with the same illnesses several years earlier.

The Rileys' attorneys say the parents are unsophisticated people who did not question the doctor. Michael Riley's lawyer, John Darrell, told the Boston Globe on February 7, 2007, that neither parent knew enough treatment to have challenged Kifuji. "You've got two poor parents here of minor means financially, of minor education," he said.

A reading of all the official reports and court documents in this case definitely indicate that be true.

As so often happens with families like the Riley's, who are covered by public health care programs, and with the great assistance of Dr Kifuji, the entire Riley family become a cash cow for the psychiatric-pharmaceutical industry, including the mother and father.

Another incentive certainly worth noting is the potential monthly income Dr Kifuji generated for herself by the legal pill-pushing to the Riley family. A 2003 study by the American Psychiatric Association found doctors could earn about \$263 an hour for holding three 15-minute medication management sessions per hour, compared to about \$156 for a single therapy session. That represents an hourly pay cut of 41% for doctors doing therapy only, the APA study said.

Critics say more blame should be focused on the prescribing doctors. "While the pharmaceutical companies certainly are getting rich providing mind-altering drugs for psychiatry's made-up mental disorders, the fault lies with the psychiatric community," says Kelly Patricia O'Meara, author of "PSYCHED OUT: How Psychiatry Sells Mental Illness and Pushes Pills That Kill".

"Until the fraud of psychiatric diagnosing is exposed," Ms O'Meara warns, "the American people will continue to hear about more and more of these tragic outcomes."

And it always goes back to the chicken and the egg theory. Was there an epidemic in this family where all 5 family members were so severely mentally ill? Or did the psychiatric-pharmaceutical industry convert them into life-long disabled customers through the administration of a powerful drug cocktail for years on end?

According to Dr Ann Blake Tracy, Director of International Coalition for Drug Awareness, and author of "Prozac: Panacea or Pandora?", she expects a person placed on one of these drug cocktails to be on disability within a 3- to 5-year window of time.

"And for a decade and a half," she says, "she has been trying to figure out how our economy will survive the skyrocketing disability rates."

The chicken and the egg theory arises a second time in this case when reviewing the allegations lodged against the parents. Were the bizarre behaviors of the parents cited in official reports and the media the result of ignorance, bad parenting or a wish to harm Rebecca? Or were the behaviors in fact brought on by the combination of drugs the parents were ingesting?

"Naturally," Ms O'Meara notes, "one has to wonder that if the entire family was being 'treated' for their alleged mental illnesses, why then didn't the drugs work?"

Dr Tracy says, "Is it absolutely possible that some of the alleged behaviors of the parents in this family could have been caused by the prescribed drugs they were taking."

She explains that the hypothesis behind these psychiatric drugs is backwards, meaning they often end up causing the conditions that they were prescribed to treat.

Leonard Frank, author of "Zyprexa: A Prescription for Diabetes, Disease and Early Death", concurs. "Psychiatrists and other physicians," he explains, "prescribe drugs in attempt to suppress objectionable conduct but the drugs often make the conduct even more objectionable, in which event the prescription is changed."

Then he explains, one drug may be substituted for another, or one or more drugs may be added to the mix, or the dosage may be decreased, or more likely increased, and this process may go on endlessly, he says.

Following Rebecca's death, the Department of Social Services placed the other two Riley children, Kaitlynne 6, and Gerald 11, in foster care and sought an independent opinion on their medical care, and doctors determined that their medication needed to be changed.

Persons injured by Serotonin Syndrome and seeking legal advice can contact the Robert Kwok Associates Law Firm, at (713) 773-3380;
<http://www.kwoklaw.com/about.php>

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