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- ▶ **The Use of Anti-Depressants  
in Children & Adolescents:  
Aspects of the Controversy**

# ▶ The Use of Anti-Depressants in Children & Adolescents: Aspects of the Controversy

## **The Complexity of the Problems Involved**

In December 2003, The United Kingdom Medicines and Healthcare Products Regulatory Agency banned all the SSRIs except Prozac, for those under 18 citing poor evidence of efficacy and a raised risk of self-harm and suicidal thoughts. This was done, after hearing the conclusions of an expert panel they set up to review the safety and efficacy of SSRIs in under 18s.

# The Use of Anti-Depressants in Children & Adolescents: Aspects of the Controversy

## FDA Public Health Advisory (03/22/04)

### **ABOUT POSSIBLE WORSENING DEPRESSION AND SUICIDALITY IN PATIENTS BEING TREATED WITH ANTIDEPRESSANT MEDICATIONS**

The Food and Drug Administration (FDA) asked manufacturers of the antidepressants mentioned below to include in their labeling an important Warning statement. It recommends the close observation of adult and pediatric patients treated with these agents for the emergence of agitation, irritability, insomnia, and other symptoms including the worsening of depression or the emergence of suicidality. It comprises the following antidepressants:

Celexa (citalopram); Effexor (venlafaxine); Lexapro (escitalopram); Luvox (fluvoxamine); Paxil (paroxetine); Prozac (fluoxetine); Remeron (mirtazapine); Serzone (nefazodone); Wellbutrin (bupropion); and Zoloft (sertraline) .

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## The Complexity of the Problems Involved

- Depression in young children, before puberty
- Children before ten or eleven can not grasp the concept of death
- An alternative theory
- Depression or bipolar disorders from adolescence onwards

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## The Complexity of the Problems Involved

- Brief discussion of the evolution of the concept of depression in DSM Manuals
- Depression as a normal affect
- Depression as an illness
- Reactive Depressions considerably more common than Endogenous Depression
- The issue of depression as an illness in children. Is it real, does not exist, or it is not clear yet

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## Endogenous vs Reactive Depression

- Somatic symptoms including constipation
- Loss of appetite (increase ?) >weight loss
- Lack of hygiene, less interest in looks
- Thoughts are slow (like moving molasses)
- Movements, speech, etc slow. No sexual interest (Adolescent remark, “the world is moving faster”)
- Hopelessness and helplessness severe
- Worse time in a.m., improves some by evening, etc
- Nearly always family history present

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## Endogenous vs Reactive Depression

- Depressions recur in over 50% of depressed patients (likely to happen in “endogenous depressions”)
- Incomplete remission of depression (partial remission) happens in over 40% of patients treated with antidepressants.

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## Endogenous vs Reactive Depression

- Then generally:
  - Doses may be increased
  - Change antidepressant
  - Second antidepressant may be added
  - A mood stabilizer may be added
  - Check thyroid & other medical conditions or medications that are being taken
  - Go to MAOIs or ECT



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## The role of pharmaceutical companies

- a) Pharmaceutical companies are a business
- b) Originally did their own research
- c) Expanded into to universities (consequences)
- d) Changes in the DSM Manuals

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## Antidepressant treatments effectiveness

- a) ECT effectiveness (rarely used now, why?)
- b) Tricyclics:
  - Helped 2/3 of patients (66%)
  - Placebos helped 1/3 of patients (33%)
  - Consequences of DSM lumping together endogenous (the real McCoy) and reactive depressions

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## Antidepressant treatments effectiveness

- The above explains well the claim of 2/3 responses i.e 1/3 are legitimate and 1/3 is a placebo response
- The not accounted for remaining 1/3 are probably a mixture of reactive (not responders to placebo) and severe endogenous depressions.
- Some pharmaceutical companies have encouraged this confusion in order to medicate everybody (whether endogenous or reactive depressions)

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## Antidepressant treatments effectiveness

- I believe that antidepressants are effective in many adult endogenous depressions
- But remember that doctors are unable to distinguish between a drug and a placebo effect, thus many feel the drugs work quite well
- They may be a good alternative to ECT in many cases

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## Antidepressant treatments effectiveness

- *In terms of children and teens*, the facts are that these drugs have by and large not proven more effective than placebos, and even in adults they only prove better than placebos in only half the studies (New York Times: Health;09/16/04 by Gardiner Harris)
- Same evidence found in **Clinical Evidence Mental Health** •
- The above has been the view of some psychiatrists for a long time

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## Pharmaceuticals Companies

- Pharmaceuticals companies have heavily promoted the use of antidepressants in younger children
- This enormously widens the antidepressant market
- Nearly 11 millions of prescriptions for antidepressants were given to children in 2002.
- In the first 6 months of 2003 that number grew by 8%

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## Pharmaceuticals Companies

- The estimated total market value of antidepressant prescriptions is \$20 billions
- That makes antidepressants one of the biggest selling drugs of all times
- In England, Seroxat (Paxil) alone, produced by GSK reached \$2.7 billions British pounds (roughly 7 billion dollars)

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## Pharmaceuticals Companies

- The question of hiding research data (negative findings or dangerous findings) from Doctors and the public
- In the US, in June, the state of New York sued GSK (Paxil) for suppressing research revealing the suicide risk for under 18s. The state received 2.5 millions and the info will be released
- The need for transparency in research results
- The confusion of issues involved



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## Suicidal Risks

- Increased suicidal risks as patients improve. Why is that the case?
- The role of cultural changes
- The role of the media (TV, newspapers, radio, internet, etc) •
- The imitation (copy cat) factor

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## Suicidal Risks

- The multiple reason why people commit suicide, including children an adolescents. Not everyone is depressed.
- I'll show you how sorry you will be (friends, parents, etc). Done out of anger
- Hemingway as an example of psychotic depression
- Cultural and religious factors

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## Suicidal Risks

- Different character structures, different personality structures
- Different abilities to tolerate frustration and to accept substitutes or change
- Most adolescent suicides are errors in judgment
- A number of depressed people will kill themselves no matter what (example: psychiatric hospitals)

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## Other Factors

- Unrealistic expectations of the power of medications and knowledge of doctors
- •The need to negate one's role in that outcome
- •The need to externalize blame when somebody dies.

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## Other Factors

- The role of the family history, severe depressions, suicides, bipolar disorders, etc
- Most children and adolescents that have killed themselves were not taking anti-depressants
- Anti-acne medications blamed some time ago

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## **Some erroneous attributions to the efficacy of antidepressants**

- 1) Endogenous depressions tended to last a given time (typical for each patient) after which the depression lifted spontaneously in most cases. Since antidepressants are given for a long time, the spontaneous remission may be attributed to the effect of the antidepressant

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## **Some erroneous attributions to the efficacy of antidepressants**

- 2) In the case of reactive depressions time has proven a great healer. The amount of time is variable according to the person ego strengths, resources, etc. Again, the “cure” can be attributed in error to the antidepressant, when it was really time, individual resources, support systems, spontaneous favorable changes in people’s life etc, that did it

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## Very recent research findings

- Three weeks after this lecture was given researches have provided evidence that, in young mice, the antidepressants (SSRIs) permanently alter the brain, resulting in a greater risk of depression and anxiety in adulthood
- Jay Gingrich and colleagues presented their findings at the Neuroscience meeting in San Diego and in Oct 29 (Science) their research suggesting that the serotonin transporter plays a pivotal role in normal brain formation, and if the transporter function is blocked (by using SSRI) while the brain is developing, the mechanisms that control mood could be permanently disrupted