

CONVERTING JAPAN & CONVERTING WOMEN TO PAXIL

June 2010

**DAVID HEALY MD
CARDIFF UNIVERSITY**

ORGANIZATION OF TERATOLOGY INFORMATION SERVICES

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Research



Antidepressant Use During Pregnancy Study

Antidepressants

Antidepressants are among the most commonly used medications during pregnancy. Little is known about the possible effects of continuing or discontinuing antidepressant use during pregnancy on the overall health of the mother and baby. This study is investigating the effect of discontinuing use of antidepressants during pregnancy on maternal behavior as well as on the cognitive and behavioral development of infants.



You can help
Call: 1-877-875-7333
toll free in Canada and the US
or contact us via email
medications.pregnancy@hotmail.com
<http://aberard.ca/>

(Please include your phone number and the best time to contact you.)



Depression Is a Dilemma for Women in Pregnancy

When Steven Mahkizadeh Allen of Marietta, Ga., learned she was pregnant, she was 43, had been married for two years, had gone through two marriages and had all but given up hope of having a baby.

But instead of being overjoyed, Mr. Allen was immobilized: panic-ridden, nauseated, listless and thoroughly depressed. She could not rouse herself to go to work in the marketing business she founded and ran, or even get through the newspaper.

And she faced the pregnant woman's quintessential

Article

Major Depression and Antidepressant Treatment: Impact on Pregnancy and Neonatal Outcomes

Katherine L. Wisner, M.D.
Dorothy K.Y. Sit, M.D.
Barbara H. Hanusa, Ph.D.
Eydie L. Moses-Kolko, M.D.
Debra L. Bogen, M.D.
Diane F. Hunker, R.N.
James M. Perel, Ph.D.
Sonya Jones-Ivy, M.D.
Lisa M. Bodnar, Ph.D.
Lynn T. Singer, Ph.D.

Objective: Selective serotonin reuptake inhibition (SSRI) use during pregnancy incurs low absolute risk for major malformations; however, other adverse outcomes have been reported. Major depression also affects reproductive outcomes. This study examined whether 1) minor physical anomalies, 2) maternal weight gain and infant birth weight, 3) preterm birth, and 4) neonatal adaptation are affected by SSRI or depressive exposure.

Method: This prospective observational investigation included maternal assessments at 20, 30, and 36 weeks of gestation. Neonatal outcomes were obtained by blinded review of delivery records and infant examinations. Pregnant women (N=298) were categorized into three mutually exclusive exposure groups: 1) no SSRI, no depression (N=131); 2) SSRI exposure (N=71), either continuous (N=48) or partial (N=23); and 3) major depressive disorder (N=96), either continuous (N=14) or partial (N=22). The mean depressive symptom level of the group with continuous depression and no SSRI exposure was significantly greater than for all other groups, demonstrating the expected treatment effect of SSRI. Main outcomes were minor physical anomalies, maternal weight gain, infant birth weight, pregnancy duration, and neonatal characteristics.

Results: Infants exposed to either SSRI or depression continuously across gestation were more likely to be born preterm than infants with partial or no exposure. Neither SSRI nor depression exposure increased risk for minor physical anomalies or reduced maternal weight gain. Mean infant birth weights were equivalent. Other neonatal outcomes were similar, except 5-minute Apgar scores.

Conclusions: For depressed pregnant women, both continuous SSRI exposure and continuous untreated depression were associated with preterm birth rates exceeding 20%.

(Am J Psychiatry 2009; 166:557-566)


Hastings Center Reports

Dec 2009

R · I · S · K and the Pregnant Body

by ANNE DRAPKIN LYERLY, LISA M. MITCHELL,
ELIZABETH MITCHELL ARMSTRONG, LISA H. HARRIS, REBECCA
KUKLA, MIRIAM KUPPERMANN, AND MARGARET OLIVIA LITTLE

Reasoning well about risks is most challenging when a woman is pregnant, for patient and doctor alike. During pregnancy, we tend to note the risks of medical interventions without adequately noting those of failing to intervene, yet when it's time to give birth, interventions are seldom questioned, even when they don't work. Meanwhile, outside the clinic, advice given to pregnant women on how to stay healthy in everyday life can seem capricious and overly cautious. This kind of reasoning reflects fear, not evidence.



G Koren 2007
The Way Women Perceive Teratogenic Risk
Can J Clin Pharmacology 14, e10-e16

BEAUTY HEALTH & FITNESS editor: Abigail Walsh

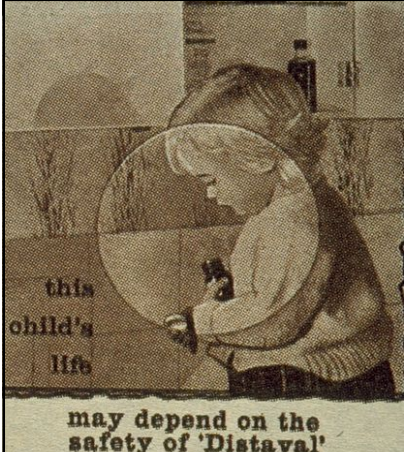


pregnant pause

With a flurry of recent reports challenging the safety of antidepressants for unborn babies, doctors and concerned mothers-to-be are rethinking the guidelines. Alexis Jetter reports.

including a small dose of Paxil, the antidepressant that she took daily to ward off panic attacks. But Fromm's doctors said she needn't worry. Her family physician ordered a copy of the *Physician's Desk Reference* to the entry on Paxil. "We read it together," Fromm recalls. "It said it was safe to take while pregnant." But just two hours after Mark

abnormalities healed on their own, while others required major surgery. But FDA officials weren't taking any chances. In December 2001, the agency issued a public advisory urging doctors not to give Paxil to pregnant women. Recent findings have sharply heightened these concerns. The U.S. Centers for Disease Control, Boston University, and the University of Montreal have all found that Paxil can triple a baby's risk of developing a heart defect like Mark Fromm's. "When my study on Paxil first came out, I was really walking on eggshells, and I was criticized," says Asak, Bernard, Ph.D., professor of pharmacy at the University of Montreal. "But now other people have done the studies, too. And I'm much more comfortable saying that Paxil is a bad drug to take during pregnancy."



1962

Thalidomide

Distaval
Contergan



TIME
THE WEEKLY NEWSMAGAZINE

Senator Estes Kefauver

Democratic Candidate for Presidency 1952/1956

Chairman of Anti-Trust Committee

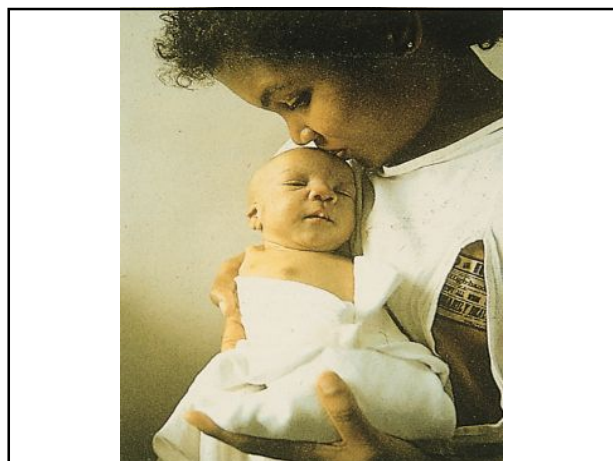
1959 Kefauver Harris Hearings

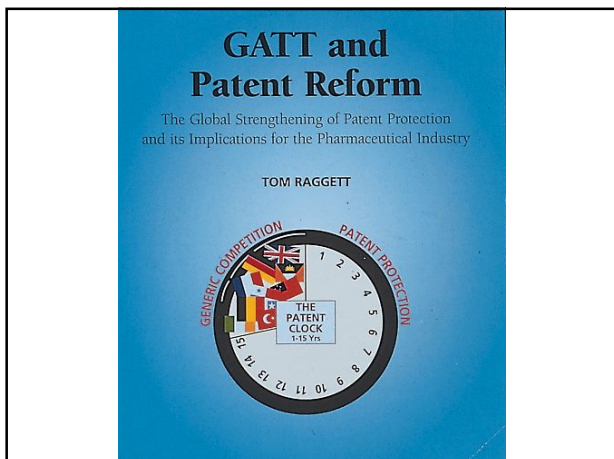
Prices Fixed and High
4 Billion pages of Adverts
Adverts Fraudulent
Withholding Safety Data

77 countries surveyed,
28 allowed product patents
Drug prices 18 to 255 times higher

“These drug fellows pay for a lobby that makes the steel boys look like popcorn vendors. ... anyone who dares seek the truth will be accused of being a persecutor”

Estes Kefauver





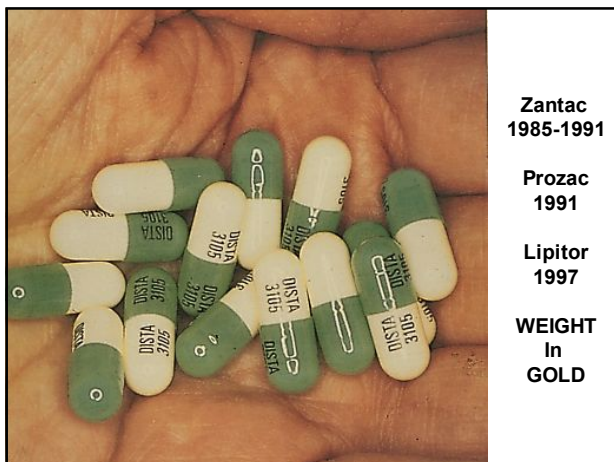
1962 Amendments

1 Prescription only Status

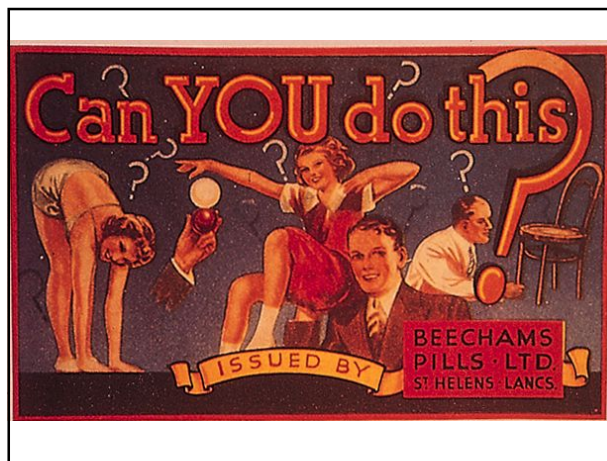
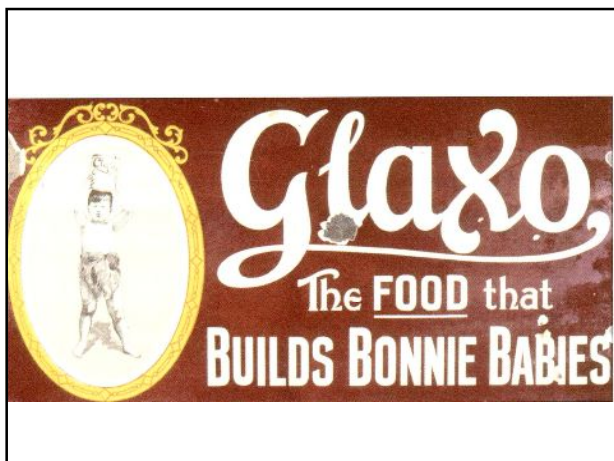
2 Controlled Trials

3 Drugs for Diseases

Product Patents - TRIPs



2007			
Worldwide	\$663.5	100%	6.1
Oncologics	41.4	6.2	16.2
Lipid regulators	33.7	5.1	-6.7
Respiratory agents	28.6	4.3	12.3
Acid pump inhibitors	25.6	3.9	2.8
Antidiabetics	24.1	3.6	10.7
Antipsychotics	20.7	3.1	10.7
Antidepressants	19.7	3.0	-6.8
Angiotensin II antagonists	19.4	2.9	13.6
Anti-epileptics	15.2	2.3	13.5
Autoimmune agents	13.3	2.0	20.3



BEECHAM'S PILLS

These renowned pills are composed entirely of Medicinal Herbs [aloes, ginger and soap]

.. Cure constipation, Headache, Dizziness, Wind, Pain, and Spasms at the Stomach, Pains in the Back, Restlessness, Insomnia, Indigestion, Want of Appetite, Fullness after Meals, Vomitings, Sickness of the Stomach, Bilious or Liver Complaints, Cold Chills, Flushings of Heat, Lowness of Spirits, and all Nervous Affections.. Pimples and Blotches on the Skin,.. **Maladies of Indiscretion**, Kidney and Urinary Disorders, and Menstrual Derangements

February 7, 1990 Leigh Thompson Memo

"I am concerned about reports I get re UK attitude toward Prozac safety. Leber (FDA) suggested a few minutes ago we use CSM database to compare Prozac aggression and suicidal ideation with other antidepressants in UK. Although he is a fan of Prozac and believes a lot of this is garbage, he is clearly a political creature and will have to respond to pressures. **I hope Patrick realizes that Lilly can go down the tubes if we lose Prozac and just one event in the UK can cost us that.**"

Her body
her choice...
...Your decision

1914
1951
1962
Because..

THE GLOBALIZATION OF THE AMERICAN PSYCHE
Crazy Like Us
ETHAN WATTERS

Converting Japan to Paxil
2000
No SSRIs
Taijin Kyofu

What it is.
What it feels like.
Your life is waiting. **PAXIL**

Has social anxiety put your life on hold?
You are not alone.
PAXIL is the only medicine proven effective for anxiety by the FDA for Generalized Anxiety Disorder.
Ask your doctor about PAXIL today... your life is waiting!

Do you suffer from social anxiety disorder?
For more information, talk to your doctor.

1. Does an unreasonable fear of embarrassment cause you to avoid most social interaction? Yes No

2. Is the anxiety you feel around people so intense it sometimes feels like a panic attack?

3. Has this overwhelming anxiety significantly impaired your work or social life?

Answering these questions and discussing them with your doctor can help determine if you suffer from social anxiety disorder. Lesser degrees of social anxiety usually do not require medication.

PAXIL
PAROXETINE HCl

YOU MAY WANT TO CUT THIS OUT AND SHOW IT TO YOUR DOCTOR.

NEW, 1ST AND ONLY SSRI FDA APPROVED FOR GAD

Overpowered by ANXIETY

Empowered by Paxil

PAROXETINE HCl

The anxiolytic at its core

NEW
FDA APPROVED FOR PTSD

Still fighting monsters

Paxil
The courage to dream

PROVEN on the CAPS-1 including all symptom clusters:

- Avoidance
- Hyperarousal
- Intrusive re-experiencing

PROVEN ACROSS TRAUMA TYPES:

- Single incident trauma
- Multiple incidents
- Sustained or repeated exposure
- Military
- Civilian

PAXIL
PAROXETINE HCl

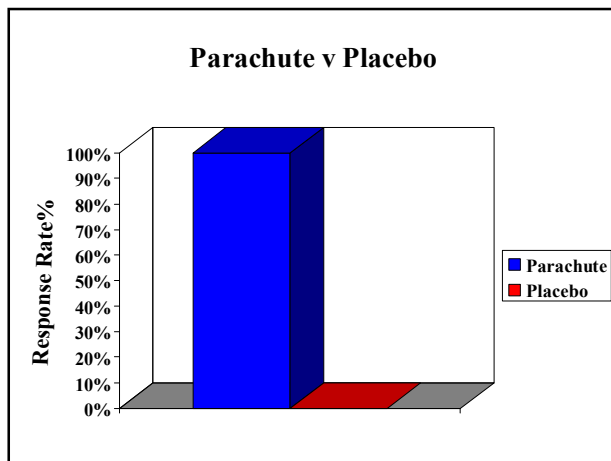
The anxiolytic antidepressant

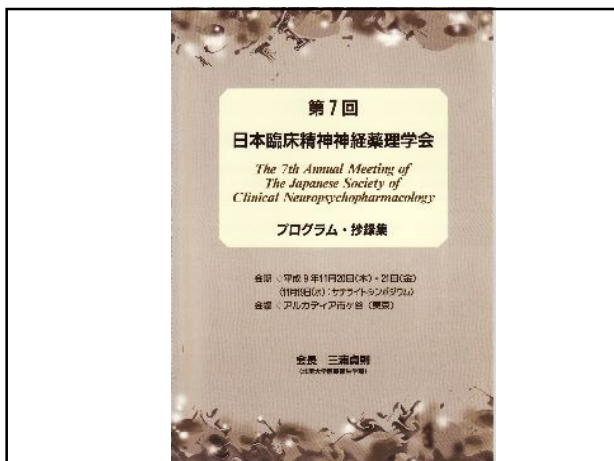
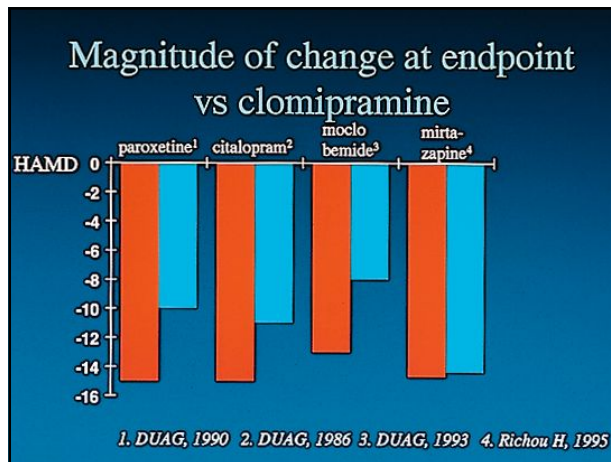
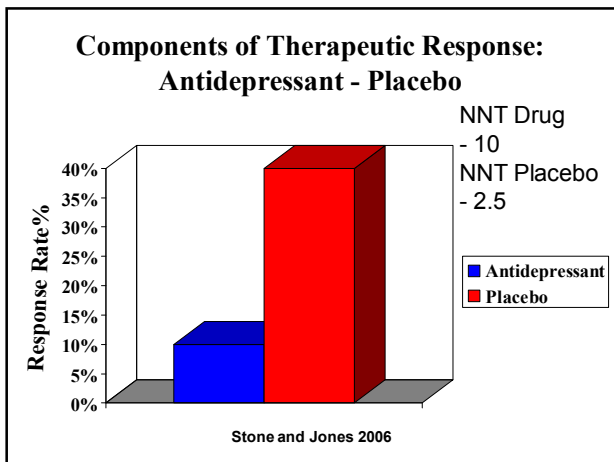
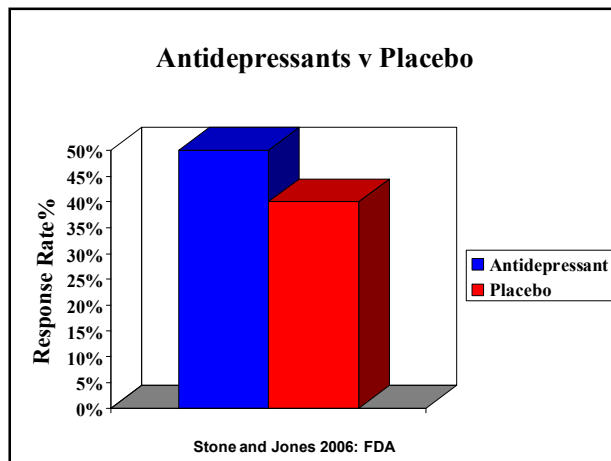
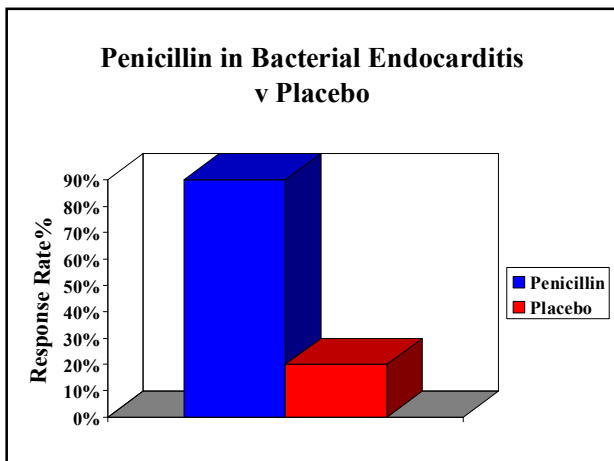
A Lunch Symposium to be held at the American Psychiatric Association 155th Annual Meeting

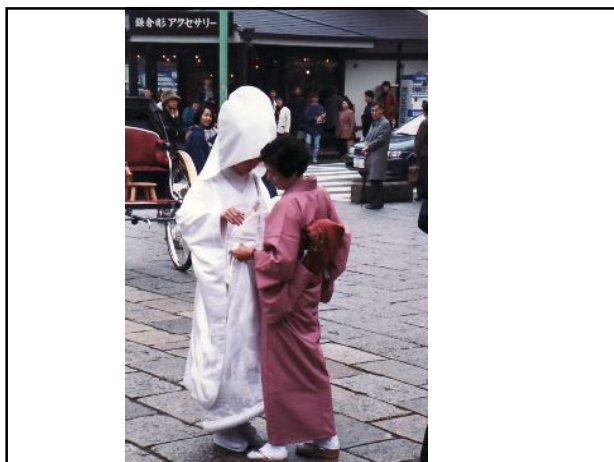
Recent Developments in the Science and Treatment of PTSD

SUNDAY, MAY 19, 2002
1:30 PM - 4:30 PM

Lucas Hotel
Millennium Hall
Second Floor







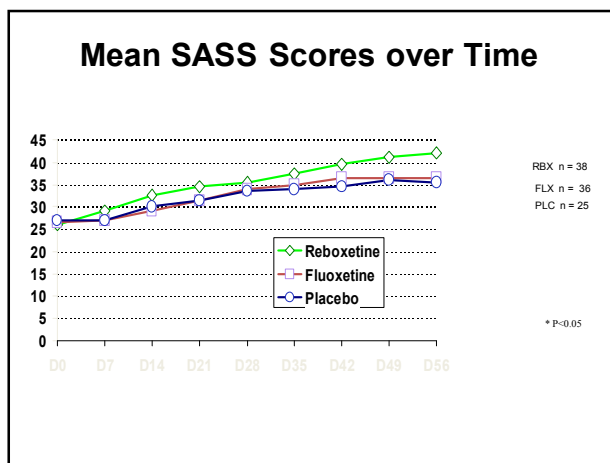
MEASURING OUTCOMES

1. Disease Specific Observer Ratings
 - Hamilton Depression Scale
2. Disease Specific Subjective Ratings
 - Beck Depression Scale
3. Disease Non-specific Observer Rating
 - Clinical Global Impression Scale
4. Disease Non-specific Subject Rating
 - Quality of Life Scales

Antihypertensives & Quality of Life

	Improved			Worse		
	Physician's Assessment	Patient's Assessment	Relative's Assessment	Physician's Assessment	Patient's Assessment	Relative's Assessment
Female	34	10	1	0	4	33
Male	41	26	0	0	3	41
TOTAL	75	36	1	0	7	74

Jachuck et al 1982



**INSTRUCTIONS FOR
PULLING RABBIT OUT OF HAT**

- 1/ PUT RABBIT IN HAT
- 2/



- Asthma – Peak Flow**
- Lipid Levels**
- Blood Glucose**
- Eating Disorders**
- Osteoporosis**
- The Measurement
is the Illness**

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APA 2007 Annual Meeting

CLINICAL SKILLS
— to —
CLINICAL SCALES:
Practical Tools in the Management of
Patients with Schizophrenia

Earn Up to 3 *AMA PRA Category 1 Credits*SM

Saturday, May 19 - 5:30 PM
Manchester Grand Hyatt, Douglas Pavilion C/D, San Diego, CA
A complimentary dinner will be served as a part of this program.

GAIN INSIGHTS ON Effective Use of Clinical Assessments Skills and Scales
Selection of Tailored Treatment Plans
Guidance for Incorporating Routine Assessments of Medical Health
to Improve Patient Outcomes
And More

Sponsored by the American Psychiatric Association. Supported by an educational grant from Pfizer, Inc.

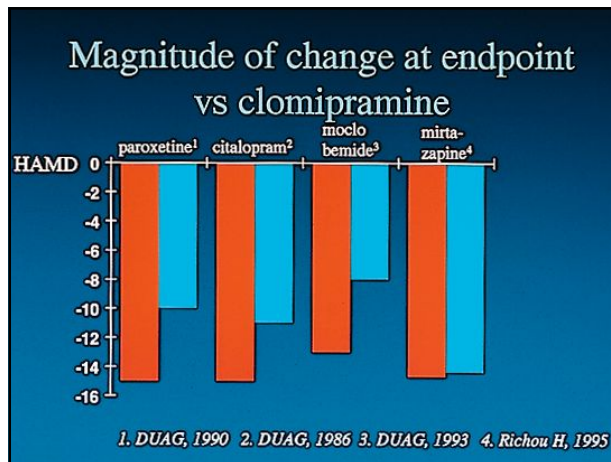
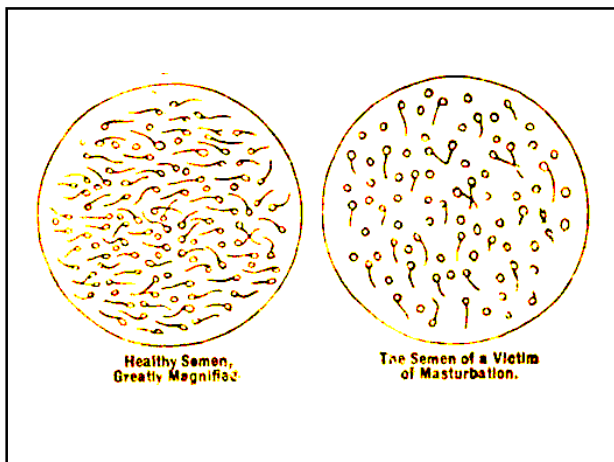
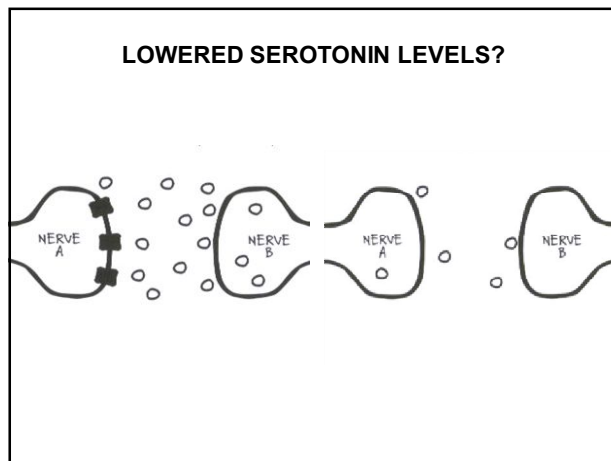


“It may be that we are witnessing a change as revolutionary as was the introduction of standardization and mass production in manufacture. Both have their positive & negative sides”.

Hamilton M (1972).

Rating Scales

- 1 Information poor checklists**
- 2 Capture of Clinical Gaze**
- 3 Measurement pseudo-science**
- 4 Informational Reductionism**



Clinical Research Organizations

Quintiles	1982
Parexel	1983
Covance	1987
\$30 Billion	

Did you know...that of the world's top 30 best-selling drugs, Quintiles helped develop or commercialise every one?

- Trials in Undeveloped Countries
- Private Ethics
- Marketing Trials
- Data Access



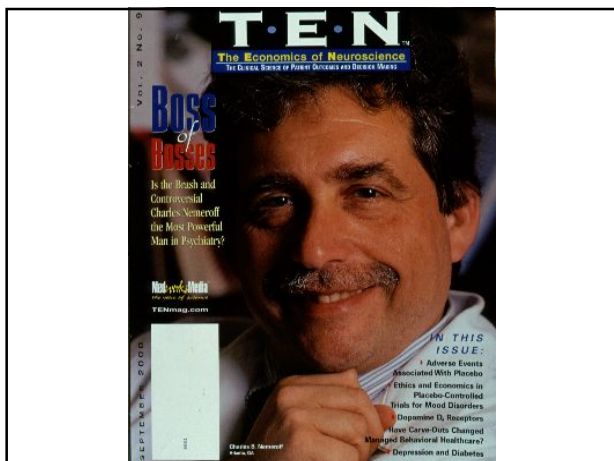
We'll work with you to formulate your objectives and focus on your key data. We'll recommend ways to expand awareness and target the audience, media or journals that will best fit your goals.

- PIVOTAL STUDY REPORTS
- SCIENTIFIC MEETING ABSTRACTS AND POSTERS
- CLINICAL STUDY REVIEWS
- PROMOTIONAL FORMULARY KITS
- PRODUCT-SPECIFIC MONOGRAPHS
- JOURNAL PROCEEDINGS/SUPPLEMENTS
- ROUNDTABLE MEETINGS
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Need to know who are the respected experts in the field served by your new product? If we don't already know them, we'll find them; and we'll help you build a relationship that serves everyone's needs.



From 2000 through 2006, Dr. Nemeroff earned more than \$960,000 from GlaxoSmithKline but listed earnings of less than \$35,000 for the period on his university disclosure forms, according to Congressional documents.

New York Times April 10th 2008

Spring 2003 — Volume 37, Supplement 1

Psychopharmacology BULLETIN

<p>Alan F. Schatzkin, MD Adjunct Professor, School of Medicine Boston, MA</p> <p>Carl Stroup, MD Department of Psychiatry Columbia University Columbia, SC</p> <p>Karen Hansen-Wagner, MD, PhD University of Illinois Medical School Urbana, IL</p> <p>David S. Walitkin, MD Medical Center of Illinois Health Urbana, IL</p>	<p>6 Introduction Charles B. Nemeroff, MD, PhD</p> <p>8 Neuropharmacology of Paroxetine Michael J. Owen, PhD, and Charles B. Nemeroff, MD, PhD</p> <p>19 In Vivo Neuroimaging Correlates of the Efficacy of Paroxetine in the Treatment of Major Depressive Disorder Gloria Abate, PhD</p> <p>29 Pharmacokinetic, Drug Interaction, and Tolerability of Paroxetine and Paroxetine CR C. Emily Cohen, PhD</p> <p>42 Paroxetine Treatment of Major Depressive Disorder Maris A. Galis, MD</p> <p>53 Treatment of Panic Disorder: Focus on Paroxetine Mark H. Pollack, MD, and Alicia C. Doyle, MD</p> <p>64 Paroxetine Treatment of Generalized Anxiety Disorder David F. Tolin, MD, PhD, and C. Emily Cohen, PhD</p> <p>76 Treatment of Postmenopausal Stress Disorder: The Impact of Paroxetine Joanne B. Trossman, MD</p> <p>89 Obsessive-Compulsive Disorder: Implications of the Efficacy of an SSRI Paroxetine Philip T. Pincus, MD</p> <p>97 Advances in Recognition and Treatment of Social Anxiety Disorder: A 10-Year Retrospective Barbara K. Davis, MD, PhD, PhD</p> <p>108 Paroxetine Use in Medication-Resistant Patients Steven G. Cole, MD, PhD, Robert J. Swenson, MD, Andrew Miller, MD, and Christopher J. Manning, MD, PhD</p> <p>123 Paroxetine Treatment of Depression in Law Enforcement Charles P. Reynolds III, MD</p> <p>135 Paroxetine Treatment of Mood Disorders in Women: Premenstrual Dysphoric Disorder and Hot Flashes Kimberly A. Yonkers, MD</p> <p>148 Clinical Management of Perinatal Depression: Focus on Paroxetine D. Jeffrey Newport, MD, MSCR, MDiv, and Zachary N. Stowe, MD</p> <p>167 Paroxetine Treatment of Mood and Anxiety Disorders in Children and Adolescents Karen Hansen-Wagner, MD, PhD</p> <p>176 Efficacy and Tolerability of Controlled-Release Paroxetine Robert G. Giblin, MD</p>
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Psychopharmacology Bulletin, Spring 2003, Vol. 37, Suppl. 1

135 Paroxetine Treatment of Mood Disorders in Women: Premenstrual Dysphoric Disorder and Hot Flashes
Kimberly A. Yonkers, MD

148 Clinical Management of Perinatal Depression: Focus on Paroxetine
D. Jeffrey Newport, MD, MSCR, MDiv, and Zachary N. Stowe, MD

THE WALL STREET JOURNAL. Digital Network

THE WALL STREET JOURNAL. HEALTH

June 10, 2009

Emory Psychiatrist Cited in Conflicts of Interest

Article | Comments (2) | MORE IN HEALTH

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Emory University has disciplined a prominent psychiatrist who was being paid by an antidepressant maker at the same time he was conducting federal research about the use of such drugs in pregnant women.

The university said its medical school dean issued a letter of reprimand on April 30 to psychiatrist Zachary Stowe related to his "external relationships." Dr. Stowe was instructed to immediately eliminate conflicts related to current federal grants and was barred from having any conflicts for the next...

The senator [Grassley] said records he obtained from GlaxoSmithKline PLC, the maker of the antidepressant Paxil, indicated Dr. Stowe was paid \$154,400 by the drug company in 2007 and \$99,300 during the first 10 months of 2008. The totals included payments for at least 95 promotional talks on behalf of the company.

"Strong evidence is a compelling and truly original work of reporting and analysis, uncovering America's role in legitimizing how the world delivers violence and health."
—The Honorable, Senator of Massachusetts

— THE —
GLOBALIZATION
OF THE
AMERICAN PSYCHE

Crazy Like Us

ETHAN WATTERS

**Japan
2000**

No SSRIs

Pregnancy

THE ANTIDEPRESSANT OF CHOICE FOR WOMEN

**Japan
2000**

No SSRIs

Pregnancy

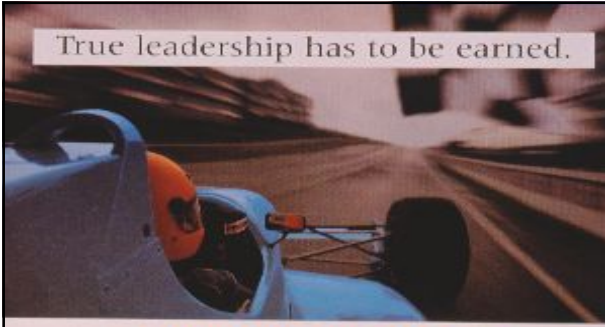
**Paxil
Seroxat
Paroxetine**

Depression in Women:
Times for Special Consideration

- Premenstrual
- Pregnancy
- Postpartum
- Perimenopause
- Postmenopause

Short half life
Lactation
Untreated depression

True leadership has to be earned.



REDUCING THE RISK OF DISCONTINUATION SYNDROME

Prozac is rarely associated with the unpleasant symptoms of antidepressant Discontinuation Syndrome. Maybe that's why Prozac has earned its status around the world.

THE JOURNAL OF CLINICAL PSYCHIATRY

Volume 68 1997 Supplement 7

SUPPLEMENT

Antidepressant Discontinuation Syndrome: Update on Serotonin Reuptake Inhibitors

Celebrating Over 50 Years of Service to Psychiatry

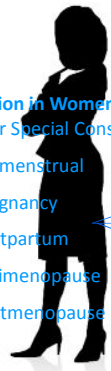
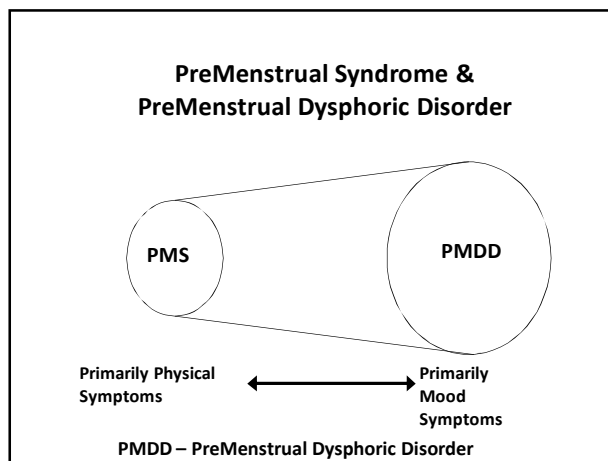
THE ANTIDEPRESSANT OF CHOICE FOR WOMEN

**Paxil
Seroxat
Paroxetine**

**Depression in Women:
Times for Special Consideration**

- Premenstrual
- Pregnancy
- Postpartum
- Perimenopause
- Postmenopause

Short half life
Lactation
Untreated depression

PreMenstrual Dysphoric Disorder

Background	Symptoms
<ul style="list-style-type: none"> • 75% of women report minor, isolated, occasional premenstrual changes • 20 – 50% report “premenstrual syndrome” • 3 – 8% of reproductive-age women have PMDD 	<ul style="list-style-type: none"> • Anxiety, irritability, tension • Affective lability • ↓ Interest • ↓ Energy, fatigability • Food craving • Bloating, breast tenderness, headaches, joint pain

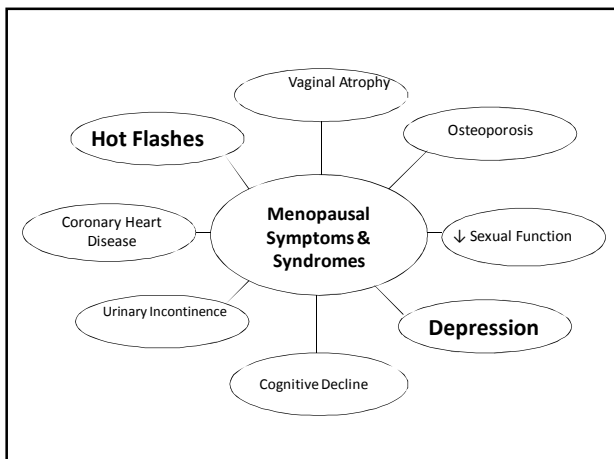
JOURNAL OF WOMEN'S HEALTH
Volume 15, Number 3, 2006
© Mary Ann Liebert, Inc.

Expert Guidelines for the Treatment of Severe PMS, PMDD, and Comorbidities: The Role of SSRIs

MEIR STEINER, M.D., Ph.D.,¹ TERI PEARLSTEIN, M.D.,² LEE S. COHEN, M.D.,³ JEAN ENDICOTT, Ph.D.,⁴ SUSAN G. KORNSTEIN, M.D.,⁵ CARLA ROBERTS, M.D., Ph.D.,⁶ DAVID L. ROBERTS, M.D.,⁷ and KIMBERLY YONKERS, M.D.⁸

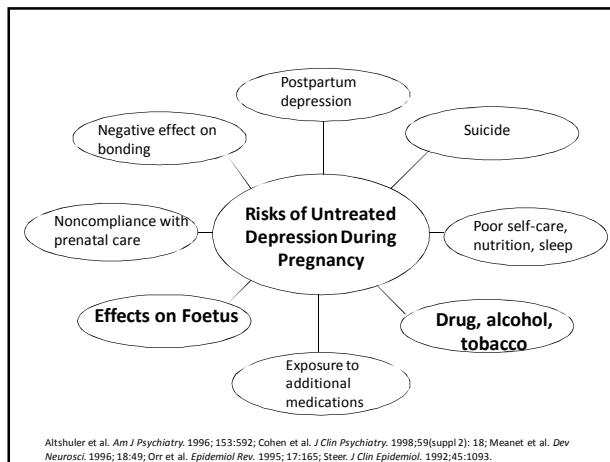
ABSTRACT

The hallmark feature of premenstrual syndrome (PMS) and premenstrual dysphoric disorder (PMDD) is the predictable, cyclic nature of symptoms or distinct on/offness that begins in the late luteal phase of the menstrual cycle and remits shortly after the onset of menstruation. PMDD is distinguished from PMS by the severity of symptoms, predominance of mood symptoms, and role dysfunction, particularly in personal relationships and marital/family domains. Several treatment modalities are beneficial in PMDD and severe PMS, but the selective serotonin reuptake inhibitors (SSRIs) have emerged as first-line therapy. The SSRIs can be administered continuously throughout the entire month, intermittently from ovulation to the onset of menstruation, or semi-intermittently with dosage increases during the late luteal phase. These guidelines present practical treatment algorithms for the use of SSRIs in women with pure PMDD or severe PMS, PMDD and underlying sub-syndromal clinical features of mood or anxiety, or premenstrual exacerbation of a mood/anxiety disorder.




Paroxetine For Hot Flashes In Breast Cancer Patients

- Rationale
 - 55% survivors have debilitating Hot Flashes
 - Association between Estrogen RT – breast Cancer
 - Nonhormonal treatment disappointing
 - Bellergal, clonidine, vit. E, soy products
- Mechanism?
 - estrogen withdrawal related to ↓ serotonin



About Us

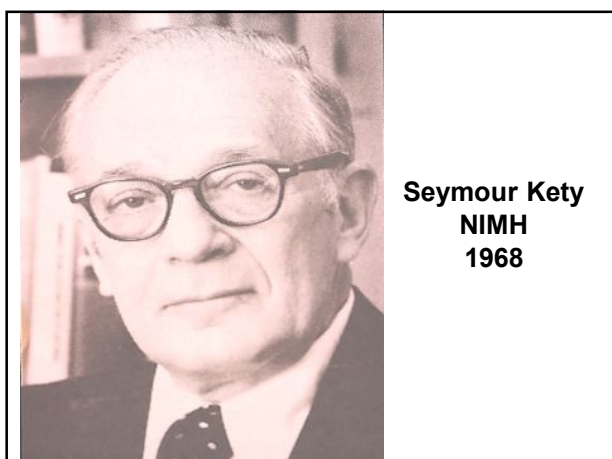


Zach Stowe

Emory Women's Mental Health Program

These 'perfect childbirth experiences' account for less than 15% of all pregnancies





“The manipulation of the brain by any of the biological techniques which can be developed in the foreseeable future would involve such drastic invasions of privacy, integrity and the unalienable rights of the individual

that in their application behavioral control would already have been achieved even if the electrodes carried no current and the pill were placebo”.

S Kety, Hearings of the National Commission on Health Sciences & Society. 90th Congress, Second Session. Page 292

 The image shows the cover of the Japanese film 'Red Cliff' (赤ひげ), featuring a man with a beard. To the right of the image, the text reads:

Medicine & Markets

1. Collect the Right Data – Patient/Discovery
2. Access to Data – Free Market
3. Prescription Only?
4. Product Patents?