2ND ANNUAL CHAIRS IN PSYCHIATRY SUMMIT
The Master Class for Psychiatric Professional Development
Mood and Anxiety Disorders: The Complexities of Integrating Syndromes

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Disclosures

- **Research/Grants:** None
- **Speakers Bureau:** None
- **Consultant:** None
- **Stockholder:** Corcept Therapeutics, CeNeRx BioPharma
- **Other Financial Interest:** Owner of Promoter Neurosciences, LLC; Ownership of Patents: Promoter sequences for corticotropin-releasing factor CRF2alpha and method of identifying agents that alter the activity of the promoter sequences: U.S. Patent issued on 07-04-06; patent #7071323, divisional patent applied for on 9/26/2005; patent application #11/234916; Promoter sequences for urocortin II and the use thereof: U.S. Patent issued on 08-08-06; patent #7087385; Promoter sequences for corticotropin-releasing factor binding protein and use thereof: U.S. Patent issued on 10-17-06; patent #7122650Method for reducing CRF receptor mRNA: Patent applied for on 07-22-04 patent application #20050042212
Learning Objective

Recognize the overlapping symptomatology of mood and anxiety disorders and develop an individualized treatment plan focused on sustained remission
Diagnosis, Long-Term Course, and Treatment of Generalized Anxiety Disorder (GAD): Current Knowledge and Future Directions

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Disclosures

- **Research/Grants:** Pfizer Inc.; Wyeth Pharmaceuticals
- **Speakers Bureau:** None
- **Consultant:** CeNeRx BioPharma; Cephalon, Inc.; Cypress Bioscience, Inc.; Cyberonics, Inc.; Forest Laboratories, Inc.; Janssen, L.P.; JDS, Medtronic, Inc.; Novartis Pharmaceuticals Corporation; Organon Pharmaceuticals USA Inc.; Pfizer Inc.; Roche; Solvay Pharmaceuticals, Inc.; Wyeth Pharmaceuticals
- **Stockholder:** None
- **Other Financial Interest:** None
- **Advisory Board:** Abbott Laboratories; Bristol-Myers Squibb Company; CeNeRx BioPharma; Cyberonics, Inc.; Forest Laboratories, Inc.; Janssen, L.P.; Novartis Pharmaceuticals Corporation; Organon Pharmaceuticals USA Inc.; Pfizer Inc.
Learning Objective

To identify the prevalence of GAD/MDD comorbidity and differentiate among therapeutic options for GAD
Generalized Anxiety Disorder (GAD)

- Excessive or uncontrolled worry \( \geq 6 \text{ months} \)
- 3 or more associated physical and psychological symptoms
- Causes significant distress or impairment
- Symptoms not better explained by other condition

GAD and MDD

- 42% to 70% of patients with GAD have co-existing depressive symptoms or syndromes
- GAD predicts greater risk of secondary MDD
- Compared with patients with GAD alone, those with GAD and MDD have:
  - Higher rates of suicide ideation and attempts
  - Greater impairment in all functional domains
  - Lower recovery and greater recurrence
  - Higher rates of chronicity
  - More medical comorbidity
  - Greater health care utilization and costs

Which Models Are Consistent with the Frequent Comorbidity Between GAD and MDD?

- Variations of a broader underlying syndrome erroneously separated
- Are they different phenocopies of the same genetic diathesis?
  - Different environment or experiences = different syndromes
- Disorder features are a risk factor for another disorder
- One disorder causes another?
- Are they different stages of the same illness?

Two prospective, naturalistic, longitudinal, studies of adults with anxiety disorders

Harvard/Brown Anxiety Research Project (HARP)
  - 711 mental health patients
  - Up to 14 years of data

Primary Care Anxiety Project (PCAP)
  - 539 primary care patients
  - Up to 5 years of data

Current Available GAD Medications and Psychotherapy

- **FDA-approved:**
  - Benzodiazepines, buspirone
  - SSRIs: paroxetine, escitalopram
  - SNRIs: venlafaxine, duloxetine

- **Evidence from RCTs (not FDA-approved):**
  - SSRIs: fluvoxamine, sertraline, citalopram
  - TCAs: imipramine
  - Hydroxyzine, trazodone, pregabalin, tiagabine

- **Cognitive Behavioral Therapy (not FDA-approved)**

Combining Benzodiazepines with Antidepressants

Potential Benefits:

- Provide rapid anxiolysis during antidepressant lag
- Decrease early anxiety associated with antidepressant initiation
- Treat residual anxiety after successful antidepressant treatment
- Combination of a benzodiazepine and an antidepressant may be more effective than monotherapy

Cognitive behavioral therapy (CBT) is a well-established treatment for GAD, SAD, and panic disorder. Specific CBT treatments for each disorder all include similar components of:

- Psychoeducation regarding anxiety
- Restructuring anxiety-related cognitions
- Exposure to avoided situations
- Possible use of relaxation techniques

Pharmacologic Treatments Under Development
(These Agents Are Not FDA-Approved for GAD)

- Neuroactive peptides
- Selective GABA reuptake inhibitors
- $\alpha_2\delta$ ligands
- $\text{GABA}_A$-receptor modulators
- Newer 5-HT$_{2A}$ receptor agonists
- Others?

GAD: Summary

- Protracted time to recovery
- Rapid time to recurrence
- Often chronic course (> 5-year episodes)
- High rates of comorbidity (MDD) and subsyndromal symptoms
- Significant impairment in social and physical functioning
- Enormous economic burden on society
- Improve therapeutics essential for **acute** episodes and **maintenance treatment** for GAD patients with and without comorbid MDD
Reproductive Endocrine-Related Depression: One Size Does Not Fit All

David R. Rubinow, MD
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Disclosures

- **Research/Grants:** Foundation of Hope; National Institutes of Health; National Institute of Mental Health
- **Speakers Bureau:** None
- **Consultant:** Azevan Pharmaceutical, Inc.; Dialogues in Clinical Neuroscience
- **Stockholder:** Amgen Inc.; Vanguard Special Health Mutual Fund
- **Other Financial Interest:** None
- **Advisory Board:** None
Learning Objective

Identify 2 issues that are relevant to reproductive endocrine-related depression at different reproductive stages and explain their clinical implications.
“I’m pregnant, doc. Should I continue taking my antidepressant?”
### Retrospective vs. Prospective Documentation of Prenatal Depression

<table>
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<th>Retrospective Recall of Depression During Pregnancy</th>
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<tr>
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**Statistics**

Fisher’s Exact: \( p < .0001, k = 0.42 \)  
[95% CI: 0.30 – 0.55]

NCI = confidence interval; PV = negative predictive value; PPV = positive predictive value

“Now that I’m perimenopausal, what do you have for my libido, doc?”
E₂ Replacement Does NOT Restore Libido

DISF = Derogatis Interview of Sexual Functioning-Self Report
Hormone-Related Changes in Sexual Interest

* p < .05

Effect of Baseline Sexual Interest Scores on Sexual Interest Across Treatment Phase

Effect of Baseline Sexual Interest Scores on Sexual Interest Across Treatment Phase

Women

DISF Total Score

Lo Libido (n = 6)  Hi Libido (n = 6)

<.01

"I got depressed when I was perimenopausal. The HRT did the trick, but will I be OK if I stop it now?"
Reproductive endocrine-related depression in women is a potential concern at all stages of adult life

- **Pregnancy**
  - Concerns about fetal exposure to ADs and other medications
  - Depression during pregnancy

- **Perimenopause**
  - $E_2$ replacement does not restore libido

- **Postmenopause**
  - $E_2$ withdrawal precipitates depressive symptoms in asymptomatic women with past PMD
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Breier A, Charney DS, Heninger GR. Major depression in patients with agoraphobia and panic disorder. Arch Gen Psychiatry 1984;41:1129-1135.


