

## 1-800-PSYCH

- If you are obsessive-compulsive, dial 1 repeatedly...
- If you are paranoid-delusional, dial 2 and wait, your call is being traced...
- If you are schizophrenic, a little voice will tell you what number to dial...
- If you have MPD, dial 3 if you are Alice, dial 4 if you are John, dial 5 if you are Rossana Roces...
- If you are manic, dial 1-9 100 times...
- If you are depressed, any number will do.... Nobody will answer anyway.

## What is Clinical Depression?

- It is a biologically-based brain disorder that affects one's thoughts, feelings, behavior and physical health;
- It is an affective disorder, which means that changes in mood occurs in the depressed patient.

## Symptoms of Depression

- DSM-IV Criteria for Major Depressive Episode
  - Symptoms that during the same 2-week period, there has been a change in the functioning due to:
  - Persistent feelings of sadness or anxiety
  - Loss of interest or pleasure in usual activities

## Symptoms of Depression

- DSM-IV Criteria for Major Depressive Episode
  - Changes in appetite resulting in weight loss or gain not related to dieting
  - Insomnia or oversleeping
  - Loss of energy or increased fatigue
  - Restlessness or irritability
  - Feelings of worthlessness or inappropriate guilt
  - Difficulty in thinking, concentrating or making decisions
  - Thoughts of death or suicide or attempts at suicide
  - Not due to other conditions (medical, hormonal problems)
  - Not due to substance abuse or side effects of medications

## Depression:

### Common Symptoms

### A Guide to Rapid Assessment

- S – Sleep
- P – Psychomotor retardation/agitation
- A – Appetite
- C – Concentration
- E – Energy
- D – Depressed mood
- I – Interest

- G – Guilt
- S - Suicidality

What causes Depression?

- Several factors play a role in the onset of depression.
- Biochemistry – deficiencies in 2 chemicals in the brain – serotonin and norepinephrine

What causes Depression?

- Genetic – depression can run in families. For example, if one identical twin has depression, the other twin will have a 70% chance of having the illness sometime in life.

What causes Depression?

- Personality – people with low self-esteem, who are overwhelmed by stress or who are generally pessimistic.

What causes Depression?

- Environmental Factors – continuous exposure to violence, neglect abuse or poverty.

Risk Factors for Depression

- Gender
- Marital Factors
- Previous Episode
- Heredity
- Age – depression usually occurs between the ages of 20 and 50, people over the age of 65 maybe especially vulnerable

Why does depression in the older population go untreated/undetected

- The depressed older person mistakes his symptoms for dementia or the normal aging process
- Families don't recognize the symptoms of depression
- Many families aren't aware that depression is a medical illness
- Fear of stigmatization
- Fear of costly treatment
- Side effects of some medications (e.g. anti-hypertensives)

Risk Factors for Major Depression

- Gender – approximately 20-25% of women and 12% of men will experience a serious depression at least once in their lifetime:
  - Women seek more treatment
  - Women tend to be more under stress
  - Women maybe more prone to depression because of the possible effects of hormones
  - Men suppress their depression thru alcohol or other substances (Masked depression)

Depression Co-Occurs with Medical Illness

- The rate of major depression among those with medical illness is significant.

- In primary care, estimates range from 5-10%.
- Among medical in-patients, the rate is 10-14%.
- Research has shown that major depression occurs in:
  - Between 40-65% of patients who have had an MI
  - They may also have a shorter life expectancy than non-depressed MI
  - Approximately 10-27% of post-stroke patients

#### Depression Co-Occurs with Psychiatric Disorders

Between 50-70% of eating disorder patients have a lifetime history of major depressive disorder.

#### Depression Co-Occurs with Substance Abuse Disorders

Substance abuse disorder are present in 32% of patients with depressive disorders

Annals of Internal Medicine

15 March 1997

**“Primary Care Clinicians fail to diagnose depression in half of their patients who have the condition. When detected, clinicians provide adequate treatment only half of the time. Because 5% to 10% (of medical in-patients) have major depression, this indictment is alarming.”**

#### Challenge to the Detection of Depression in the Medical Setting

Time

–Most outpatient visit last 15 minutes or less; whereas visits to a specialist typically lasts 30 minutes or longer

#### Challenge to the Detection of Depression in the Medical Setting

Somatization

–Medical patients with mental disorders typically present with fatigue, insomnia, pain, GI symptoms or other symptoms

#### Challenge to the Detection of Depression in the Medical Setting

Co-morbid medical disorders camouflage depression by sharing somatic symptoms

#### Challenge to the Detection of Depression in the Medical Setting

#### Stigmatization

#### Challenge to the Detection of Depression in the Medical Setting

Cost of outpatient and in-patient visits

Major Clinical Features differentiating Pseudodementia from Dementia

*Clinical Course and History*

*Complaints and Clinical Behavior*

*Clinical Features related to Memory, Cognitive and Intellectual Dysfunction*

Neuron

Dopamine AutoReceptors

Receptor Sensitivity

Receptor Sensitivity

Site of Drug Action at the Synapse

## Pharmacotherapy in Depression

- Antidepressants
  - Tricyclics and tetracyclics – *imipramine*
  - SSRI's = *fluoxetine, sertraline, paroxetine*
  - Newer antidepressants
  - SER-NE reuptake inhibitors
  - NA and SER neurotransmission
  - MAOI's
  - Neuroleptics (for psychotic depression)
  - Dopamine receptor antagonist (TYPICAL)
  - Serotonin-Dopamine antagonist (TYPICAL)
  - Mood Stabilizers (Lithium) and anticonvulsant medications
- ### ANTIDEPRESSANTS

- Selective enhancement of NE activity
  - Selective enhancement of 5HT activity
  - Nonselective enhancement of both NE and 5HT activity
  - Unknown: no potent effects on NE and 5HT activity
- ### Selective Serotonin Reuptake Inhibitors

## Monoamines and Depression

- A role for 5HT and NE in depression was suggested following studies that proved manipulation of monoamine levels could either induce or alleviate the symptoms of depression

## Monoamines and Depression

- Depression results from reduced availability of 5HT and/or NE
- ### CLASSIFICATIONS OF ANTIDEPRESSANTS BY PUTATIVE MECHANISMS OF ACTION RESPONSIBLE FOR ANTIDEPRESSANT EFFICACY
- Serotonin and norepinephrine reuptake inhibition plus effects on multiple receptors and fast sodium channels (Amitriptyline, Imipramine)
  - Selective serotonin reuptake inhibitors (Fluoxetine, Paroxetine, Sertraline, Fluvoxamine)
  - Selective norepinephrine reuptake inhibition (Desipramine)
  - Serotonin and Norepinephrine reuptake inhibition (Venlafaxine)
  - Serotonin (5HT<sub>2A</sub> and 2C) and norepinephrine uptake inhibition (Nefazodone)
  - Serotonin (5HT<sub>2A</sub> and 2C) and norepinephrine (alpha 2) receptor blockade (Mirtazapine)
  - Dopamine and norepinephrine reuptake inhibition (Bupropion)
  - Monoamine oxidase inhibition (Tranylcypromine, phenelzine)

Algorithm for treating patients with major depressive disorder:

Perskorn SH, Burke M: Somatic Therapy for Major Depressive Disorder. J Clin Psychiatry 53: 10, 1992

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Rationale for the Combined Use of a Noradrenaline and Serotonin Reuptake Inhibitor

- Antidepressants produce down-regulation of beta-adrenoceptors only after chronic (14 days) administration
- Rapid down-regulation of beta-adrenoceptors is thought to be associated with an earlier onset of antidepressant effect
- Preliminary studies have shown a rapid down-regulation with the combination of desipramine (noradrenaline reuptake inhibitor) and fluoxetine (serotonin reuptake inhibitor)

Clinical Studies of Efexor  
on Special Groups of Patients

- Elderly patients (efficacy)
- 92 patients aged 64 & above, Efexor vs. dothiepin
- Results: At week 6, Efexor had better response rates than dothiepin.
- Suicide ideation scores on MADRS decreased significantly more on the Efexor than on the dothiepin group.

Clinical Studies of Efexor  
on Special Groups of Patients

- Elderly patients (safety & efficacy)
- 116 elderly depressed patients in the General Practice setting
- Efexor dose was 102mg to 108mg/day
- Results: Therapy was continued for 6 months in 73% of patients  
–therapy was continued for 12 months in 66% of patients  
–80% of patients reported a rating of “much or very much improved” in 12 months

Clinical Studies of Efexor  
on Special Groups of Patients

- Patients w/ psychomotor agitation or retardation
- Meta-analysis of 5 placebo-controlled double blind studies
- Results:  
–Significant improvement on the HAM-D retardation was observed in patients with Efexor compared to patients on placebo or imipramine, beginning at week 3

-Significant improvement on the HAM-D agitation item was observed in patients with Efexor compared to patients on placebo or imipramine, beginning at week 1

#### Clinical Studies of Efexor on Special Groups of Patients

- Patients w/ treatment-resistant or refractory depression
- 84 patients (hospitalized and out-patients) with depression refractory treatment with 3 antidepressants
- Mean dose of Efexor: 245mg/day
- Results: By week 8, mean HAM-D & MADRS scores decreased by 42% & 39%, respectively
- By week 12, about 1/3 of patients were considered partial or full responders with Efexor

#### Clinical Studies of Efexor on Special Groups of Patients

- Effect of Efexor on sleep
- 24 hospitalized depressed patients
- Results: Efexor had important neurophysiological effects, particularly
  - early and steady suppression of Rapid Eye Movement (REM) sleep
  - absence of sedating and overactivating effects

#### Venlafaxine Safety Profile

- Safety profile similar to SSRIs
- Relatively safe in overdose
- few clinically significant laboratory abnormalities
- Dose-related increase in BP; mainly at doses above 200 mg/day
- Well tolerated in long-term trials
- Well tolerated in the elderly
- Weak inhibitor of P450IID6
- Combined use with MAOIs is contraindicated

#### Summary

- SNRIs represent a new class of antidepressant with selective effects on serotonin and noradrenaline reuptake
- SNRIs have demonstrated
  - efficacy in a broad range of patients (inpatients, melancholia, refractory, elderly)
  - the potential for an improved response with an increased dose
  - the potential for early onset of activity
  - a tolerability profile similar to the SSRIs

The place of the HPA axis and hippocampus in the pathophysiology of affective disorders.

The physiology of the HPA Axis

### **New Understanding and Management in the field of DEPRESSIVE DISORDERS**

- The concept of depression: sporadic revolution or continuous evolution?
  - N. Sartorius (Switzerland)
- The place of the HPA axis and hippocampus in the pathophysiology of affective disorders.
  - B.S. Evans (USA)
- Comorbidity and mixed anxiety-depressive disorders: Clinical curiosity or pathophysiological need?
  - H.U. Witchen (Germany)

### Summary

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    - a tolerability profile similar to the SSRIs
- Patients need to know -

- That depression is not due to weakness of character
- That depression is a medical illness
- That depression needs medications

### The Typical Course of Depressive Disorders and the Phases of Treatment

#### Key concepts of antidepressant side effects

- Antidepressants are equal in efficacy but differ in terms of side effects and safety
- Side effects account for two-third of treatment discontinuation

#### General Principles in

#### Anti-Depressant Treatment

- Drug choices
  - All the main drugs appear to have broadly similar efficacy and so anti-depressant choice will be based upon:
    - Features of the depression
    - Suicide risk
    - Concomitant therapy
    - Concurrent illness
    - Side-effect tolerability
    - Cost and special considerations

Side Effect & Drug Interactions Associated with Neurotransmitter Receptor Blockade  
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