Depression: Diagnosis and Treatment

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“The sorrow which has no vent in tears may make other organsweep.”

Henry Maudsley, MD
1835-1918

Depression vs. Demoralization

- Transplant expectations were not met
- Transplant medications destabilize mental illness especially depression and bipolar illness
- Ongoing medical illness, pain, fatigue make diagnosis difficult
- Medical illness masked psychiatric illness
Depression: 5 clusters of symptoms

- 1. Vegetative: Sleep, appetite, sex
- 2. Cognitive: Concentration, attention, memory
- 3. Impulse: Suicide, homicide
- 4. Behavioral: Motivation, interest
- 5. Physical: Headaches, GI symptoms, muscle tension

Prevalence of major depression in chronic medical illness

- Prevalence of major depression:
  - Community sample: 2% to 4%
  - Primary-care setting: 5% to 10%
  - Inpatient medical setting: 6% to 14%
- Medically-ill patients:
  - 41% higher prevalence rate of recent psychiatric illness
  - 28% lifetime rate of major depression


Prevalence of major depression in chronic medical illnesses

<table>
<thead>
<tr>
<th>Condition</th>
<th>Prevalence</th>
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<tbody>
<tr>
<td>Multiple sclerosis</td>
<td>6% to 57%</td>
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<tr>
<td>Stroke</td>
<td>30% to 50%</td>
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<tr>
<td>Cancer (inpatients)</td>
<td>42%</td>
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<tr>
<td>Parkinson’s disease</td>
<td>40%</td>
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<tr>
<td>Diabetes mellitus</td>
<td>33%</td>
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<tr>
<td>Coronary artery disease</td>
<td>18% to 26%</td>
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<tr>
<td>Post-myocardial infarction</td>
<td>16% to 18%</td>
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Depression and cardiovascular mortality following myocardial infarction

- The overall mean increase in risk is 4.1
- Range = 2.3 to 7.5
- Depression is equal to ventricular dysfunction as a mortality risk factor
- Most of the mortality risk occurs in the first 6 months
- Mortality risk seems to be proportionate to the severity of depression


6 & 18 Month Mortality Following Myocardial Infarction

6 months 18 months

% of coronary deaths

Non-depressed Depressed


THREE TREATMENT PHASES

- Acute: 6–12 weeks
- Continuation: 4–9 months
- Maintenance: 1 or more
Recognize depression

Screen with 2 questions:
■ 1. During past month have you been feeling down, depressed or hopeless?
■ 2. Have you lost interest or pleasure?
■ If yes to both questions, follow up with clinical interview: SPACE (less specific) DIGS (more depression specific)

“SPACE DIGS”

■ Sleep
■ Psychomotor: Agitation, slowing
■ Appetite
■ Concentration
■ Energy
■ Depressed mood
■ Interest
■ Guilt
■ Suicide

Treatment with Antidepressant

Address fear of dependency, stigma
■ Start low go slow
■ Prepare for side effects
■ Have 3 measurable goals
■ Screen for bipolar illness
■ It takes 2-6 weeks to see effects
ADHERENCE WITH ANTIDEPRESSANT THERAPY

In primary care treatment of depression:
- 25%–28% stop therapy within 1 month
- Over 40% stop within 3 months
- Underdosing is a major problem

Katon. JAMA. 1995
Lin. Medical Care. 1995

Serotonin Dysfunction

- There are 5 serotonergic pathways
  1. Midbrain raphe to prefrontal cortex involved in depression
  2. Midbrain raphe to basal ganglia involved in movement and obsessive compulsive disorder
  3. Midbrain raphe to limbic cortex and hippocampus involved in panic disorder
  4. Midbrain raphe to hypothalamus involved in bulimia
  5. Midbrain raphe to spinal cord important in sexual function

Possible effects of receptor binding

- Decrease depression
- Psychomotor activation
- Antiparkinsonian effects
- Reduce suicidal behavior
- Antipsychotic effects
- Hypotension
- Ejaculatory dysfunction
- Sleep
- Protect sexual function
- Reduce depression
- Antianxiety effects
- GI disturbances
- Sexual dysfunction
- Tachycardia
- Dizziness
- Reflexive tachycardia
- Postural hypotension
- Urinary retention
- Dry mouth
- Blurred vision
- Constipation
- Sinus tachycardia
- Sedation
- Drowsiness
- Weight gain
- Tremors
- Priapism
- Erectile/ejaculatory dysfunction
- Memory dysfunction
- ACh block
- Alpha1 block
- Alpha2 block
- H1 block
- DA reuptake inhibition
- NE reuptake inhibition
- 5HT reuptake inhibition
- 5HT block
- M1 block
- H1
- SRI
- NRI
Doxepin (Sinequan)

- Common use: Insomnia, itching and neuropathic pain
- Dose: 10-50mg qhs
- Side effects: Constipation, dry mouth, dizziness

What’s so “S” about “S”SRIs?
Sertaline (Zoloft)
- Use: Depression, dysthymia, anxiety disorder
- Safe in medically ill due to minimal drug interactions and good cardiovascular profile
- Dose: 50-300mg qd
- Start with 12.5-25 mg in elderly or ill patients
- Metabolism: 2D6 inhibition minimal, T1/2: 24 hrs
- Side effects: Nausea, indigestion, diarrhea, sexual dysfunction

Paroxetine (Paxil)
- Use: Depression, panic disorder
- Dose: 10-60mg qd
- Metabolism: Potent 2D6 inhibitor, will increase levels of beta-blockers, inhibits conversion of codeine to morphine, half-life: 20hrs
- Side effects: Dry mouth, constipation, sedation, sexual, withdrawal

Fluoxetine (Prozac)
- Use: Depression, OCD, Bulimia
- Dose: 20-80mg qd
- Metabolism: Potent 2D6 inhibition, metabolite, Norfluoxetine, inhibits 3A4 which will lead to increased cyclo, FK and prednisone levels, Half-life 72 hrs
- Side effects: Restlessness, anxiety, GI, sexual dysfunction
Citalopram (Celexa)
- Use: Depression, anxiety disorders
- Dose: 10-60mg qd
- Side effects: Mild insomnia, anxiety, headache, sexual
- Minimal drug interactions, safe in medically ill patients, well tolerated

Venlafaxine (Effexor-XR) 75-450 mg
Duloxetine (Cymbalta) 60-120mg

Bupropion (Wellbutrin-XL) 300-450 mg
Mirtazapine (Remeron) 15-45 mg

Lorazepam (Ativan)

Anxiety and insomnia
1-2 mg po bid, titrate up until anxiety is relieved
- IM Ativan should not exceed 4mg per dose
- 1mg Ativan is equal to 10mg of Librium, 5mg Valium, 1.25mg of Versed, or 0.25 mg of Klonopin
- Conjugation reaction only, no oxidation or hydroxylation. There are no active metabolites. It can be used in patient with active alcoholic hepatitis. Half-life: 12 hrs, peak plasma level 2 hrs

Clonazepam (Klonopin)

Long-acting benzodiazepine used for anxiety, mania, steroid induced anxiety disorder
0.5 mg –1mg po q 12 hrs, maximum dose 8mg a day
- Only comes in tablet form, usually given as a bid drug
- Reduction, hydroxylation and oxidation
- Half-life: 34 hrs
- Less abuse potential, easier to taper