Dual Diagnosis: Substance Abuse and Mental Illness

and a review of the major PSYCHIATRIC MEDICINES

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Special appreciation to Gary L. Viale, Pharm D., BCPP, FCSHP
"I think the dosage needs adjusting. I’m not nearly as happy as the people in the ads."
Psychopathology

• Psychopathology refers to problematic patterns of thought, feeling, and behavior
  – Disrupted functioning at home, work, and in the person’s social life
  – Patterns that cause distress in the person or in others
  – Psychopathology literally means sickness of the mind

• Psychopathology varies between and within cultures
Psychological Disorders Commonly Seen in Addictions Treatment

- Schizophrenia
- Mood disorders
  - Bipolar disorder (manic depression)
  - Depressive disorders
- Anxiety disorders
Descriptive Diagnosis

- Abnormality is reflected in discrete symptoms

- As in physical illness, symptoms fall into discrete clusters called syndromes

- Syndromes are assumed to have discrete causes and are to be treated using different therapies
DSM-IV

• The American Psychiatric Association published a diagnostic manual that attempts to classify signs and symptoms into syndromes
  • Signs are observable phenomena (temperature)
  • Symptoms are reports from patients (headache)

• The current edition is termed the DSM-IV
  • The DSM-IV uses a multi-axial system of diagnosis
    – The axes cover symptoms as well as medical conditions, stress, and current level of function
# The Axes of DSM-IV

<table>
<thead>
<tr>
<th>Axis</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>I</td>
<td>Presenting Symptoms causing distress</td>
</tr>
<tr>
<td>II</td>
<td>How the person carries themselves throughout their life</td>
</tr>
<tr>
<td>III</td>
<td>Medical conditions that may be relevant to understanding or treating a psychological disorder</td>
</tr>
<tr>
<td>IV</td>
<td>Psychosocial and environmental problems</td>
</tr>
<tr>
<td>V</td>
<td>Global assessment of functioning (GAF)</td>
</tr>
</tbody>
</table>

(Source: DSM-IV, American Psychiatric Association, 1994)
Pharmacotherapy

- Psychotropic medications are drugs that act on the brain to alter mental function

- Prior to 1956, schizophrenia was virtually untreatable with many patients confined for life in mental hospitals
  - Chlorpromazine (Thorazine) was found to reduce severity of psychotic thought, allowing people to live outside of mental institutions
Impact of Chlorpromazine on Institutionalization

(Figure adapted from Davis, 1985)
Psychotropic Mechanisms of Action

• Psychotropic drugs can alter behavior via:
  – An interaction with neurotransmitters in brain
    • Some release specific transmitters
    • Some block the reuptake of transmitters
    • Some interact with postsynaptic receptors
    • Some may act within neuron cells
  – A placebo effect
    • Subjects believe in the efficacy of the drug and show an actual change in function (analgesia or relief from pain shows moderate placebo effects)
Some Diagnoses Influenced By Serotonin Dysfunction

- Eating/Sexual Disorders
- OCD/PTSD
- Appetitive/Dysfunctionitive Obsessionality
- Panic Disorder
- Anxiety
- Mood
- Major Depression
- Aggression/Suicide
- Psychosis
- Behavioral/Personality Disorders
- Schizophrenia/Psychotic Mood Disorders
Some Diagnoses Influenced By Dopamine Dysfunction

- Impaired movement/muscle coordination
- Major Depression/Anhedonia
- Behavioral/Personality Disorder
- Schizophrenia/Psychotic Mood Disorders
- Aggression/Suicide
- Psychosis

Dopamine
Some Diagnoses Influenced By Norepinephrine Dysfunction

- Neuropsychological
  - Behavioral/Personality disorders

- Mood
  - Major Depression

- Anxiety
  - Panic disorder

- Psychosis
  - Schizophrenia/Psychotic Mood Disorders

Norepinephrine
Some Diagnoses Influenced By Opioid Peptides Dysfunction

- Neuroendocrine
  - Distress
  - Pain Syndromes
- Mood
  - Major Depression
- Psychosis
  - Schizophrenia/Psychotic Mood Disorders
- Autonomic
  - Autonomic Distress
  - Blood Pressure
  - Body Temperature

Opioid Peptides
Mechanism of Actions

(a) Decreases neural transmission by "locking up" receptor sites

(b) Increases neural transmission by blocking reuptake

(c) Increases neural transmission by blocking breakdown of neurotransmitters in synaptic vesicles

Neurotransmitters released

Drug binds with receptors to prevent them from being activated by the neurotransmitters in the synapse.

Drug blocks neurotransmitters from being taken back into the presynaptic membrane, leaving the neurotransmitters in the synapse longer.

Drug prevents the neurotransmitter returning from the synapse from being broken down for storage, which keeps it available at the synapse.
Co-Occurring Disorders

*Dual diagnosis* is a term describing those persons who suffer from co-occurring mental illness and substance abuse disorders.
Prevalence

• 19.4 million (9.2%) adults with a substance abuse disorder

• 19.2 million (9%) adults with independent mood disorders including major depression, dysthymia, manic depression

• 23 million (11%) adults with independent anxiety disorders

Prevalence

• Roughly, 50% of individuals with severe mental illness are affected by substance abuse

• 37% of alcohol abusers and 53% of drug abusers have at least one serious mental illness

• Of all people diagnosed as mentally ill, 29% abuse alcohol and other drugs
Prevalence

• An estimated 50% of homeless adults with serious mental illnesses have a co-occurring substance abuse disorder.

Prevalence

• 47% of schizophrenics also have a substance abuse disorder (4x the general population)

• 61% of people with bipolar disorder also have a substance abuse disorder (more than 5x that of the general population)

Prevalence

• The drugs most commonly used is alcohol followed by marijuana, cocaine and methamphetamine.

• Prescription sedative and pain killer drugs are also abused in this population.
Prevalence

• Have a higher risk for hospitalization, violence, depression, suicide, homelessness, HIV infection and incarcerations.
Justice Services

• 16% of jail and prison inmates are estimated to have serious mental and substance abuse disorders.

• Among detainees with mental disorders, 72% also have a co-occurring substance abuse disorder.

Suicide and AOD Use

- Psychoactive drugs are present at autopsy in 30–50% of suicides
- Intoxication predisposes to suicide in those at risk by:
  - disinhibiting usual constraints on the person
  - providing ‘courage’
  - clouding judgement and the ability to see alternatives
  - deepening mood or worsening psychosis
  - misadventure.
Why Such a High Rate?

• High-risk use of AODs can precipitate or exacerbate mental health problems:
  – psychosis in the mentally vulnerable (esp. from cannabis and stimulants)
  – depression (esp. from alcohol)
  – anxiety / social and phobia / panic attacks (esp. alcohol & benzodiazepines)

• Shared underlying causes / antecedents
  – genetics
  – environmental influences

• ‘Self-medication’ hypothesis

Problematic AOD use and mental health problems share many antecedents.
Co-Occurring Disorders: So What?

- Increased rates of violence (perpetrator and victims)
- Homelessness
- Poor treatment compliance
- Reduced or potentiated effect of medication
- Slower recovery from AOD-related problems
- Higher suicide rates.
Some Explanations for Co-occurring Disorders

1. Substance induced temporary disorders
2. Substances intensify prior psychiatric conditions
3. A few psychiatric disorders increase the risk for substance use disorders
• Drugs can cause psychiatric symptoms
• These last days to weeks
• They clear spontaneously
Time Frames for Symptom Abatement with Abstinence

- Depression and anxiety due to alcohol dependence: 4–6 weeks (maybe longer)
- Psychosis due to amphetamines and/or cannabis: 7–10 days
- Prolonged symptoms beyond these periods suggest an underlying mental health problem.
Schizophrenia

- Schizophrenia refers to a profound disturbance in human function including:
  - **Thought**: Illogical thought systems (delusions) and loosening of associations
  - **Perception**: Presence of hallucinations
  - **Language**: Word salad, disconnected ideas
  - **Affect**: Emotion (often flat or absent)

- Symptoms can be viewed as:
  - **Positive**: Delusions are an added function
  - **Negative**: Signal the absence of a function (flat affect)
Epidemiology of Schizophrenia

- 1% of lifetime prevalence (over 2,000,000 Americans)
- 200,000 new cases per year in USA
- 300,000 acute schizophrenic episodes annually
- 0.025 – 0.5% of total population treated for schizophrenia in any one year
- 2/3 of these require hospitalization
- More prevalent than Alzheimer’s disease, multiple sclerosis, insulin-dependent diabetes
Dopamine and Schizophrenia

• The positive symptoms of schizophrenia reflect too much brain dopamine activity
  – Antipsychotic drugs are effective antagonists of dopamine receptors (block the action of dopamine)
  – Drugs such as amphetamine release dopamine from terminals; too much amphetamine exposure can induce a psychotic state in humans

• Negative schizophrenic symptoms may reflect brain damage.
Schizophrenia: How antipsychotic meds work

**Decreased** activity prefrontal cortex (negative symptoms)

**Increased** activity mesolimbic structures (positive symptoms)
## Schizophrenia: Core Symptoms/Spectrum Disorder

<table>
<thead>
<tr>
<th>Positive Symptoms</th>
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</thead>
<tbody>
<tr>
<td>Delusions</td>
</tr>
<tr>
<td>Hallucinations (hearing)</td>
</tr>
<tr>
<td>Disorganized speech</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Negative Symptoms</th>
</tr>
</thead>
<tbody>
<tr>
<td>No emotions</td>
</tr>
<tr>
<td>Unmotivated</td>
</tr>
<tr>
<td>Nothing pleasurable</td>
</tr>
</tbody>
</table>
Substance Use Disorders Among Schizophrenics
Lifetime Risks: General Population

- Schizophrenia 1%
- Nicotine dependence 28% men & women
- Alcohol dependence 12% men, 5% women
- Marijuana dependence 5%
- Cocaine dependence 2%
Lifetime Risks: Schizophrenic Population

- Nicotine dependence 70%
- Alcohol dependence 37%
- Marijuana dependence 23%
- Cocaine dependence 13%
Consequences

- General population
- Special issues in schizophrenics
Consequences of Alcohol in General Population

- Intoxication: Poor judgment, anger, violence, impaired coordination
- Medical complications: Cardiomyopathy, anemia, cirrhosis
- Hallucinations
- Delirium tremens
Consequences of Alcohol in Schizophrenics: Special Issues

- Small amounts have greater effect
- Alcohol can increase cognitive deficits and enhance depression
Consequences of Methamphetamine in the General Population

• Myocardial infarction
• Arrhythmias
• Cerebrovascular accident
• Chestpains (when smoked), dyspnea, hyperthermia, chest X ray normal
• Paranoia
• Mood swings
• Depression (severe)
Consequences of Methamphetamine in Schizophrenics: Special Issues

• Destabilization and symptoms reemergence
• Frequent rehospitalizations
• Increased odds of violent behavior
• Increased risk of HIV infections
• Poor overall treatment compliance
Combined Methamphetamine and Alcohol Use

- Direct toxic effect on myocardium
- Increased risk of panic states
- Increases duration of elevated blood pressure (hypertension crisis)
To produce an effect:

1. A drug must bind to and interact with receptors (located on cell membranes)
2. Receptors are usually located on the surface of neurons
3. Drug-receptor binding leads to a change in the functional properties of the neuron
Receptors for Drug Action

**Receptor:** a large molecule (usually a protein) present on the surface of or within a cell.

Neurotransmitters: biologically active, naturally occurring endogenous compounds produce their effects by binding to receptors.

**EXAMPLE**
- Serotonin (5-HT) is a neurotransmitter that binds to more than 25 different serotonin receptor proteins.
  - Each receptor has a small difference in amino acid composition. They have been named as 5-HT1, 5-HT2, 5-HT2a, etc.
  - A given drug can bind to one or multiple receptors.
Understanding receptor subtypes allows for the development of new medications that are more selective in where they target their action causing fewer side effects.
Resulting in improved patient medication compliance!
Compliance Improvements Can Mean:

- Napa State Hospital
- Inpatient Acute
- Skilled Nursing Facility
- Crisis Residential
- Group home or family
Receptor Subtypes

Subtype-selective drugs

Non-selective drugs

Desired effect

Side effects

Side effects

Side effects
Ziprazidone (Geodon)

**POSITIVE SYMPTOMS**
- **D$_2$ - Antagonism**
  - Efficacy in positive symptoms
- High 5-HT$_{2A}$/D$_2$ - Affinity ratio
  - Antipsychotic efficacy, reduced EPS (compared to D$_2$ antagonism alone)

**NEGATIVE SYMPTOMS**
- 5-HT$_{2A}$ - Antagonism
  - Efficacy in negative symptoms

**OVERALL SYMPTOMS**
- 5-HT$_{2C}$ - Antagonism
  - Antipsychotic activity

**COGNITIVE AND DEPRESSIVE SYMPTOMS AND SYMPTOMS OF SOCIAL IMPAIRMENT**
  - 5-HT$_{1A}$ - Agonism
    - Antidepressant and anxiolytic activity and improved cognition
  - 5-HT$_{1D}$ - Antagonism
    - Efficacy in depressive symptoms
Anti-psychotic Medications

- Clozaril (clozapine)
- Risperdal (risperidone)
- Zyprexa (olanzapine)
- Seroquel (quetiapine)
- Geodon (ziprasidone)
- Abilify (aripiprazole)
- Invega (paliperidone)
Antipsychotic Medications

Haldol ® (haloperidol)

Geodon ® (ziprazidone)

Clozaril ® (clozapine)

Seroquel ® (quetiapine)

Zyprexa ® (olanzapine)

Risperdal ® (risperidone)

Abilify ® (aripiprazole)
Depression and Antidepressant Medications
Epidemiology of Depressive Disorders

• High rate of occurrence
• 5% lifetime prevalence
• 10 – 14 million people in U.S. depressed in a given year
• Episodes of long duration
• > 50% rate of occurrence
• Morbidity comparable to angina and advanced coronary artery disease
• High mortality from suicide
Criteria for Major Depressive Syndrome

- Depressed mood and/or loss of interest or pleasure (pervasive for 2 weeks)

- 4 of the following symptoms (3 with both depressed mood and loss of interest or pleasure)

<table>
<thead>
<tr>
<th>Physical</th>
<th>Psychologic</th>
</tr>
</thead>
<tbody>
<tr>
<td>- Sleep disorder</td>
<td>- Low self esteem/guilt</td>
</tr>
<tr>
<td>- Appetite change</td>
<td>- Poor concentration</td>
</tr>
<tr>
<td>- Fatigue</td>
<td>- indecisiveness</td>
</tr>
<tr>
<td>- Psychomotor agitation/retardation</td>
<td>- Thoughts of death/ suicidal ideation</td>
</tr>
</tbody>
</table>
Depressive Disorders: How antidepressant meds work

Predominantly lower levels of dopamine and serotonin in the brain

Decreased activity throughout the brain but focus on mesolimbic structures
## Antidepressant Medication Side Effect Concerns

<table>
<thead>
<tr>
<th>CNS</th>
<th>Sexual Function</th>
</tr>
</thead>
<tbody>
<tr>
<td>Activation</td>
<td><strong>decreased libido</strong></td>
</tr>
<tr>
<td>- insomnia</td>
<td>- impotence</td>
</tr>
<tr>
<td>- anxiety</td>
<td>- ejaculation disorder</td>
</tr>
<tr>
<td>- nervousness</td>
<td>- anorgasmia</td>
</tr>
<tr>
<td>- agitation</td>
<td></td>
</tr>
<tr>
<td>- tremor</td>
<td></td>
</tr>
<tr>
<td>Sedation</td>
<td><strong>Other</strong> (anticholinergic)</td>
</tr>
<tr>
<td>- somnolence</td>
<td>- dry mouth</td>
</tr>
<tr>
<td>- fatigue</td>
<td>- increased sweating</td>
</tr>
<tr>
<td></td>
<td>- urinary retention</td>
</tr>
<tr>
<td>GI</td>
<td></td>
</tr>
<tr>
<td>- nausea</td>
<td></td>
</tr>
<tr>
<td>- constipation</td>
<td></td>
</tr>
<tr>
<td><strong>weight gain</strong></td>
<td></td>
</tr>
<tr>
<td>- dyspepsia</td>
<td></td>
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</tbody>
</table>
Depression Is A Highly Treatable Disorder

Antidepressants are successful in 65% - 80% of all cases!

Best when combined with counseling therapy
Preferred Uses of Antidepressant Medications

- Sedative Hypnotic
- Migraine
- Fibromyalgia & DPNP
- Severe Depression
- Pain

Cymbalta

Several Commonly Used Antidepressant Medications

- **Tricyclics**
  
  Elavil, Tofranil, Anafranil, Pamelor, Norpramin, Sinequan

- **MAOIs**
  
  Nardil, Parnate, Marplan, Emsam

- **SSRIs**
  
  Prozac, Paxil, Zoloft, Luvox, Lexapro, Celexa

- **Miscellaneous Antidepressants**
  
  Effexor, Wellbutrin, Remeron, Desyrel (trazodone), Serzone, Cymbalta
# Antidepressant Medications (SSRIs)

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Prozac®</th>
<th>Paxil®</th>
<th>Zoloft®</th>
<th>Luvox®</th>
<th>Lexapro®</th>
<th>Celexa®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Picture</td>
<td><img src="image" alt="Prozac®" /></td>
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<td><img src="image" alt="Luvox®" /></td>
<td><img src="image" alt="Lexapro®" /></td>
<td><img src="image" alt="Celexa®" /></td>
</tr>
<tr>
<td>Generic Name</td>
<td>fluoxetine</td>
<td>paroxetine</td>
<td>sertraline</td>
<td>fluvoxamine</td>
<td>escitalopram</td>
<td>citalopram</td>
</tr>
</tbody>
</table>
# Antidepressant Medications

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Effexor®</th>
<th>Serzone®</th>
<th>Remeron®</th>
<th>Wellbutrin®</th>
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<tbody>
<tr>
<td>Picture</td>
<td><img src="image1.png" alt="Effexor®" /></td>
<td><img src="image2.png" alt="Serzone®" /></td>
<td><img src="image3.png" alt="Remeron®" /></td>
<td><img src="image4.png" alt="Wellbutrin®" /></td>
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<tr>
<td>Generic Name</td>
<td>venlafaxine</td>
<td>nefazodone</td>
<td>mirtazapine</td>
<td>bupropion</td>
</tr>
</tbody>
</table>
# Antidepressant Medications (TCAs)

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Tofranil®</th>
<th>Norpramin®</th>
<th>Elavil®</th>
<th>Aventyl®; Pamelor®</th>
<th>Sinequan®; Zonalon®</th>
<th>Anafranil®</th>
</tr>
</thead>
<tbody>
<tr>
<td>Picture</td>
<td><img src="image1.png" alt="Tofranil" /></td>
<td><img src="image2.png" alt="Norpramin" /></td>
<td><img src="image3.png" alt="Elavil" /></td>
<td><img src="image4.png" alt="Aventyl" /></td>
<td><img src="image5.png" alt="Sinequan" /></td>
<td><img src="image6.png" alt="Anafranil" /></td>
</tr>
<tr>
<td>Generic Name</td>
<td>imipramine</td>
<td>desipramine</td>
<td>amitriptyline</td>
<td>nortriptyline</td>
<td>doxepin</td>
<td>Clomipramine (5-HT)</td>
</tr>
</tbody>
</table>
### Antidepressant Medications

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Surmontil®</th>
<th>Vivactil®</th>
<th>Ludiomil®</th>
<th>Asendin®</th>
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<td><img src="image3.png" alt="Picture" /></td>
<td><img src="image4.png" alt="Picture" /></td>
</tr>
<tr>
<td>Generic Name</td>
<td>trimipramine</td>
<td>protriptyline</td>
<td>maprotiline</td>
<td>amoxapine</td>
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</table>
## Antidepressant Medications (MAOIs)

<table>
<thead>
<tr>
<th>Brand Name</th>
<th>Parnate®</th>
<th>Nardil®</th>
<th>Marplan®</th>
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<tbody>
<tr>
<td>Picture</td>
<td><img src="image1.png" alt="Parnate®" /></td>
<td><img src="image2.png" alt="Nardil®" /></td>
<td><img src="image3.png" alt="Marplan®" /></td>
</tr>
<tr>
<td>Generic Name</td>
<td>tranylcypromine</td>
<td>phenelzine</td>
<td>isocarboxazid</td>
</tr>
</tbody>
</table>
Bipolar Disorder and Mood Stabilizers
Epidemiology of Bipolar Disorder

- Prevalence: 1% of U.S. population (2.7 million people)
- Cause: Genetics plus developmental, social, cultural and environmental event.
- Peak Age of Onset: 15 – 19 years
- Mean Age of First Tx: 22 years
- Mean Age of First Hospitalization: 26 years
- Course of Illness:
  - High morbidity and mortality
  - Recurrent in most cases
Criteria for Mania

A. Mood abnormally elevated, expansive or irritable
B. At least 3 of the following symptoms:
   1. Grandiosity
   2. Decreased need for sleep
   3. Pressured speech
   4. Flight of ideas
   5. Distractibility
   6. Increase in activity’
   7. Activities – resulting in painful consequences
C. Marked impairment in occupational functioning
D. No delusions or hallucinations for as long as 2 weeks in the absence of prominent mood symptoms
Bipolar I Disorder:
How anti-mania (mood stabilizer) meds work

Increased activity throughout various brain areas
Treatment for Bipolar Disorder

Mood Stabilizers:

Lithium (Eskalith and others)
Tegretol (carbamazepine)
Depakote (divalproex, valproic acid)
Topamax (topiramate)
Lamictal (lamotrigine)
Trileptal (oxcarbazepine)
Mood Stabilizers

- Depakene®/Depakote® (divalproex sodium)
  - Depakene®
    - 250 mg
  - Depakote®
    - 125 mg
    - 250 mg
    - 500 mg
    - 125 mg

- Eskalith® (lithium carbonate)
  - 450 mg
  - 300 mg

- Lamictal® (lamotrigine)
  - 25 mg
  - 100 mg
  - 200 mg

- Tegretol® (carbamazepine)
  - 100 mg
  - 200 mg

- Topamax® (topiramate)
Side Effect Profile:

- Lithium toxicity looks like drunkenness but no smell of alcohol.
- Lithium (Lithium carbonate) requires close monitoring of blood levels.
- Antipsychotic medications are sometimes used as anti-mania drugs in combination with mood stabilizers (I.e. Zyprexa, Seroquel).
Long Term Prognosis of Bipolar Disorder

• Untreated, high morbidity/mortality rates
  - 20 –25% attempt or commit suicide
  - Overall functional impairment great

• Lifetime rate of substance abuse is 50 –60%
  - Requires identification and therapy for both disorders

• Treatable disorder for high percentage of patients
  - Balance between side effects and control possible
  - On-going relationship with provider important
Co-occurring Disorders Can Be Treated Effectively

Integrated Treatment for Dual Diagnosis:
Treat both conditions concurrently
Recovery refers to...

- The process by which people are able to live, work, learn, and participate fully in their communities

- The ability to live a fulfilling and productive life despite a disability

- A reduction or complete remission of symptoms

- The ability to help make important decisions affecting one’s own life.