Outlines for Unit 3 - Mood Disorders

Instructor: June Sprock
Unit 3 - Mood Disorders

Reading: Dubovsky, Davies & Dubovsky (2004) Ch 6: Mood Disorders from Hales & Yodofsky; DSM-IV chapter on Mood Disorders

I. Introduction and Overview

A. Brief Historical Review:
   1. Hippocrates
   2. Pinel
   3. Kraepelin: manic-depression

B. Description of mood disorders and case examples
   1. Depression as a symptom vs clinical syndrome
      a. major depression
      b. dysthymia
   2. Mania, hypomania, and cyclothymia

C. Diagnosis and assessment of depression
   1. Self report measures: BDI, DACL, Hopkins, Zung
   2. Rating scales: GAS, Hamilton
      a. Bagby et al. (2004): review of literature on Hamilton Rating Scale for Depression: concluded poor psychometric properties of some items (poor test-retest and inter-rater reliability; poor content validity), response options flawed, time to revise the scale (developed in 1950s)

D. Epidemiology and Course
   1. depression: common, 10-20% lifetime
   2. bipolar: rarer, <1% bipolar I, 1/2% bipolar II

E. Gender differences:
   1. mainly for depression: 2-4 times higher in women: Weissman & Klerman (1977); McGrath et al. (1990); Sprock & Yoder, 1997; Nolen-Hoeksema (2001); Kuehner (2003)
   2. Some differences in bipolar disorder: Tondo & Baldessarini, 1998; Nair et al., 2000
II. Classification and subtypes of mood disorders

Reading: Parker (2000); Parker et al. (2002); Rappaport et al. (2002); Hayden & Klein (2001); Klein & Santiago (2003)

A. Subtypes in the literature
   1. Parker (2000):
      a. historical one vs two depression controversy (unitary vs binary model of depression)
      b. hierarchical model with different factors leading to psychotic, melancholic, non-melancholic dep
      c. spectrum model to distinguish between non-melancholic subtypes
      a. Psychotic vs. Neurotic (symptoms)
      b. Endogeneous vs. Reactive (cause)
      c. Bipolar vs. Unipolar; sx, etiology, tx response
         1) family history: Winokur ('79); Tsuang et al ('80)
         2) treatment response: Goodwin ('86)
         3) Gershon et al ('82) continuum: Normal–Unipolar–Bipolar–Schizoaffective
            (based on genetics- will look at this study more specifically for etiology)
      d. Primary vs. Secondary: Robins & Guze ('70): whether pre-existing mental (or life-threatening physical) disorder
   3. Atypical depression: Parker et al. (2002)
      a. Huston & Locker ('48); West & Dally ('59)
      b. Depression + anxiety (Davidson et al., 1982): type A
      c. Atypical vegetative sx (Davidson et al., 1982): type V (what are atypical sx?)
      d. Respond to MAOIs
      e. DSM-III (1980) residual category
      f. DSM-IV atypical features specifier (like type V)
      g. Parker et al. (2002): Q current atypical specifiers in DSM-IV- lacks internal consistency; does not address anxiety component (Type A); may be a spectrum disorder with anxiety
   4. Rapid cycler: Wehr et al., 1988; Post; Tondo & Baldessarini, 1998; Nair et al., 2000
      4 or more episodes/yr; explanations: kindling process, like seizure; treatment: anti-convulsivse: tegretol
   5. Winokur’s classification: (handout)
      a. Pure depression (fam hx dep, good tx r)
      b. Depressive spectrum (fam hx alc, antisoc; variable tx resp, axis II)
6. Mathematical subtyping: factor and cluster analysis of sx: Implications for dx and treatment??
   a. Overall: anxious-tense, hostile, retarded: (from most to least frequent)
      1) BPRS, factor analysis
      2) hostile worse prognosis, blame others; retarded best resp antideps
   b. Paykel: anxious, hostile, psychotic, young w/ a pers. dis.
      1) cluster analysis; England; similar results; last group most difficult to tx

7. Akiskal's (1983, 1990) subtypes of primary dysthymia:
   a. subaffective disorder: related to mood disorder, fam hx, better resp antideps
      1) Ravindran & Lapierre: early onset, less severe=better prognos (opposite as major dep)
   b. character spectrum disorder: axis II sx, sub abuse, like Depressive pd, fam hx alc, less resp meds

B. Official classifications
   1. DSM-II (1968)
      a. Major Affective Disorder
         1) Involutional Melancholia
         2) Manic Depression
      b. Psychotic Depressive Reaction (w/ psychotic disorders)
      c. Neurotic Depression (w/ neurotic disorders)

      a. primary/secondary
      b. depression/mania

   3. RDC (1975): Spitzer, Endicott & Robins, 1975 (handout)
      Developed as part of the NIMH Collaborative Program on the Psychobiology of Depression

      a. Major Affective Disorders
         1) Bipolar Disorder
         2) Major Depression
      b. Other Specific Affective Disorders
         1) Dysthymia
         2) Cyclothymia
      c. Atypical Affective Disorders

   5. DSM-III-R (1987): introduced new term - called mood disorders (disorder of mood, not affect); new
      organization of disorders:
      a. Depressive Disorders
         1) Major Depression
         2) Dysthymia
         3) Depressive Disorder NOS
      b. Bipolar Disorders
         1) Bipolar Disorder
         2) Cyclothymia
         3) Bipolar Disorders NOS
Reading: DSM-IV; Parker (2000); Parker et al. (2002); Rappaport et al. (2002); Hayden & Klein (2001); Klein & Santiago (2003); Sato (1997)

a. Depressive Disorders: features, course, precipitants, cases
   1) Major Depression: onset 20s-40s, duration 6 mos untreated, precipitants 1st episode
      a) single episode
      
      b) recurrent
      
      c) Geller (2001): followup study of adults dx’ed dep in childhood; 1/3 developed bipolar I
      
   2) Dysthymia
      a) early vs late onset (onset before/after 21)
         (don’t dx if major dep episode before unless 2 mos remission)
         (don’t dx if major dep episode 1st 2 yrs)
      
      b) Hayden & Klein (2001): Outcome at 5 year followup:
         1) DPD features, comorbid anxiety dis or cluster C per dis, chronic stress assoc with poorer chance of recovery
         2) family hx bipolar assoc with better chance of recovery
      
   3) Klein & Santiago (2003): chronic depressions - major depression, chronic, and dysthymic disorder: associated with increased co-morbidity, worse outcome
      a) Dysthymic disorder: any age onset, 75-90% will develop major depression
      
      b) Major depression: 15-20% chronic, increase chance if early onset
      
      c) although differ in severity, chronic MD and DD both more complex, increased cumulative burden
      
   4) Depressive Disorder NOS - Examples: criteria in Appendix B
      a) Premenstrual dysphoric disorder: controversial
      
      b) Minor depression: RDC, acute, milder; Rappaport et al. (2002)
      
      c) Recurrent brief depression: < 2weeks, like major dep
      
      d) Postpsychotic depressive disorder of schizophrenia: recognize common
      
      a) first in RDC as a characterological mood disorder
      
      b) DSM-IV appendix: dx’ed as Personality Dis NOS
      
      c) substantial overlap with DD; Klein believes can be distinguished but often co-morbid, DPD can be pathway to developing DD, is associated with worse prognosis

b. Bipolar Disorders
   1) Bipolar I: more men, first episode often manic; more genetic basis than Bipolar II
      
      a) single manic episode
      
      b) most recent episode hypomanic (no code), manic/mixed, depressed or unspecified (no code)
2) **Bipolar II**: new in DSM-IV; more women, first episode often dep; 10%-> bipolar I
   a) current episode hypomanic or depressed, no present or hx of mania or mixed episodes
   b) severity: but can't use code

3) **Cyclothymia**

4) **Bipolar Disorder NOS**

**c. Specifiers for Major Depression/Bipolar:**

1) **Severity**: mild, moderate, severe w/ and w/out psychotic features (mood congruent, mood incongruent): use for major dep, manic and mixed episodes (i.e., major dep dis, bipolar I, Bipolar II); reflected in the 5th digit of the code (except for Bipolar II)

2) **Chronic**: ≥2 years: only for major depressive episodes (i.e., major dep dis, bipolar disorders only if most recent episode is depressed)
   a) **Klein & Santiago (2003)**: risk factors for chronicity: family psychopath, early adversity (abuse), DPD (low PE and high NE), ruminative response style, interpersonal conflict, chronic stress

3) **Cross-sectional symptom features** (current episode)
   a) **Melancholic features**: major depressive episode (disorders: same as above): Winokur’s pure dep, Overall’s retarded dep
   b) **Atypical features**: for major depress episode plus dysthymia; new "type V" atypical depression
      1) **Parker et al. (2002)**: Q validity, internal consistency of current features, failure to include anxiety, may represent depression-anxiety spectrum
   c) **Catatonic features**: major dep, manic or mixed episode, new to mood disorders
   d) **Postpartum onset**: major dep, manic or mixed episode, new (also for brief psychotic disorder): 1st time included any classification

4) **Course specifiers: only recurrent disorders**
   a) **Rapid cycling**: new, bipolar disorders (I or II)- 4 or more episodes (major dep, mixed, manic) past 12 mos
   b) **Seasonal pattern**: since DSM-IIIR, pattern of major depressive episodes (≥2 seasonal in past 2 yrs); for major dep dis, bipolar I or II;
      1) **Sato (1997)** review: SAD: winter vs summer depression and phototherapy; **GRETCHE**
5) **Longitudinal course specifiers: recurrent only**
   a) with or w/out full interepisode recovery
   b) with no or Superimposed on Dysthymia (DD)

d. **Mood Disorders due to a General Medical Condition**
   1) with depressive, mixed, or manic features
   2) or with major depressive-like episode

e. **Substance-induced Mood Disorders**
   1) with depressive, mixed, or manic features
   2) with onset during intoxication, withdrawal

C. **Co-morbidity:**

Reading: Mulder (2002); Hayden & Klein (2001); Klein & Santiago (2003); Cook et al. (2004); [also: skim Beutler (2000) and APA Guidelines - subsections on comorbidity]

1. **Double depression:**
   major dep superimposed on dysthymia: common; 10% dysthyms-> major depression each year; 75-90% DD develop major dep (lifetime) and 25% pts with major dep have pre-existing DD

2. **Personality disorders and depression**
   a) Gunderson & Elliot, 1985: borderline: 60% lifetime major dep
   b) Winokur, 1991: dep spectrum disorder, dep 2nd to pers dis, sub abuse
   c) Akiskal’s character spectrum disorder
   d) Overall and Paykel classifications: which ones?
   e) Depressive Personality Disorder: RDC, DSM-IV appendix as Pers Dis NOS
      1) concern that dysthymic criteria too neurovegetative (like Major Dep)- not like original concept in RDC: resulted in proposal for DPD and alternative criteria for dysthymia (both in DSM-IV appendix)
      2) Concerns about Depressive Pers Dis (DPD)
         a) overlap with dysthymia; although **Klein & Santiago (2004)**: believe can be distinguished
         b) overlap with personality disorders (especially cluster C)
         c) is it a mood disorder or a pers dis?
      3) worse prognosis (**Hayden & Klein, 2001**; Klein et al., 1993; Reich & Greene, 1991): more interpersonal diff; poorer functioning and resp to tx (meds, CBT) if DPD or DD plus DPD
   f) Some pers dis and DD (or chronic MD) may arise from similar or overlapping processes:
      1) **Klein & Santiago (2004):** increased per dis in chronic depr, possible shared genetics or liability; premorbid DPD or cluster B pers dis may be two pathways to developing chronic dep
2) Klein & Schwartz (2002): Bord PD and depr sx may arise from overlapping process in MDD; also, BPD one of most common comorbidities with DD

g) Mixed evidence for worse prognosis for depression with comorbid pers dis:

1) Durbin et al. (2000): worse prognosis for DD if comorbid cluster A or C pers dis.

2) Hayden & Klein (2001): dysthymia assoc with poorer outcome if DPD features or cluster C personality dis

3) However, Mulder (2002) review found that effect of personality disorders on outcome for major depression depended on design of the study, not always assoc with worse prognosis; high neurotic scores (FFM – includes characterological and anxiety features) predicted worse prognosis in major depression in the long term

h) different treatment proposed depression with comorbid pers dis:

1) Barber & Muentz (1996): avoidant and obs-compulsive traits in depression - cognitive-beh vs interpersonal therapy: theory of opposites (Kiesler, Benjamin circumplex models of working w/ pts w/ personality disorders)

2) However, Beutler (2000) found that insight and relationship focused tx better for internalizing pts while skill building, sx reduction best for externalizing pts

3. Overlap anxiety and mood disorders: high comorbidity

a) hard to distinguish, esp pt’s reports, clinician ratings distinguish somewhat more - WHY?

b) Mixed Anxiety-Depressive disorder – in DSM-IV appendix; dx: Anxiety Dis NOS (look at more later)

c) Joiner & Blalock (1995): increased mixed sx in women, no difference pure dep (non-clinical)


1) high overlap between anxiety and depression; therefore advocate a dimensional model

2) three dimensions in the model:
   a) negative affect (shared in depression and anxiety)
   b) positive affect (low positive affect unique to depression)
   c) autonomic arousal (unique to anxiety)  (Also called physiological hyperarousal)

3) only depression: low positive affect, high neg affect

4) only anxiety: high autonomic arousal, high neg affect

5) co-morbid dep & anxiety: low positive affect, high arousal, high neg affect; possibly higher comorbid conditions in women

6) mixed anxiety-depressive (high negative affect only): is the nonspecific overlapping component in depression and anxiety; may also be higher in women

7) will look at their model more when cover anxiety disorders

8) Cook et al. (2004): used tripartite model to examine depression and anxiety in elderly
c) **Hayden & Klein (2001):** dysthymia assoc with poorer outcome if comorbid anxiety disorder

d) **Parker et al. (2002):** anxiety features should be part of “atypical” specifier, may represent depression-anxiety spectrum

4. **Comorbidity with alcohol abuse/dependence**
   a) high comorbidity of mood disorders with substance abuse

   b) Preisig et al. (2001): comorbidity of unipolar and bipolar disorder with alcoholism

   c) often proposed as “self-medication” hypothesis, but substances can induce mood disorders; also may be a role of genetics – alcohol, substance abuse in same families as mood disorder
III. Demographic variables and mood disorders: overview and discussion

Reading: Kuehner (2003); Cocharan & Rabinowitz (2003); Nair et al. (2000); Cole & Dendukuri (2003); Cook et al. (2004)

A. Mood Disorder and Race: Discussion


<table>
<thead>
<tr>
<th></th>
<th>White</th>
<th>African Am.</th>
</tr>
</thead>
<tbody>
<tr>
<td>current major depression</td>
<td>4.8%</td>
<td>0%</td>
</tr>
<tr>
<td>current total (major + minor)</td>
<td>7.2%</td>
<td>3.8%</td>
</tr>
<tr>
<td>lifetime major depression:</td>
<td>20.8%</td>
<td>13.2%</td>
</tr>
<tr>
<td>lifetime total (major + minor):</td>
<td>27.8%</td>
<td>17.0%</td>
</tr>
</tbody>
</table>

2. Vernon & Roberts (1982): also using RDC

<table>
<thead>
<tr>
<th></th>
<th>White</th>
<th>African Am.</th>
<th>Mexican Am.</th>
</tr>
</thead>
<tbody>
<tr>
<td>current major depression</td>
<td>1.8%</td>
<td>2.1%</td>
<td>2.5%</td>
</tr>
<tr>
<td>current total (major + minor)</td>
<td>2.3%</td>
<td>4.3%</td>
<td>4.1%</td>
</tr>
<tr>
<td>lifetime major depression:</td>
<td>19.2%</td>
<td>9.6%</td>
<td>18.9%</td>
</tr>
<tr>
<td>lifetime total (major + minor):</td>
<td>25.6%</td>
<td>16.6%</td>
<td>27.0%</td>
</tr>
</tbody>
</table>

3. Kessler et al. (1994) National Comorbidity Study: lower rates mood disorders for blacks; Hispanics had higher rates than non-Hispanic whites

4. Diala et al. (2003): also using National Comorbidity Study data: >8000 adults in community; compared urban and rural: found gender diff among urban, not rural; African Am lower rate than Euro-Am

5. Ialong et al. (2004): study of urban African Am: found lower lifetime MDD (9.4%) compared studies of Euro Am, and higher rate of dep in women

6. Rushton et al. (2002): Nat. Longitudinal Study of Adolescent Health: higher rate dep in females and ethnic minority youths

7. Oquendo et al. (2001):

<table>
<thead>
<tr>
<th></th>
<th>Euro-Am</th>
<th>Afr. Am</th>
<th>Mex Am</th>
<th>Cuban Am</th>
<th>Puerto Rican</th>
</tr>
</thead>
<tbody>
<tr>
<td>1 yr prev Major Dep</td>
<td>3.6%</td>
<td>.5%</td>
<td>2.8%</td>
<td>2.5%</td>
<td>.9%</td>
</tr>
</tbody>
</table>

Suicide rate higher in men than women, but lower for Mex Am and Puerto Rican men than Euro Am men


<table>
<thead>
<tr>
<th></th>
<th>Euro-Am</th>
<th>Afr. Am</th>
<th>Hispanic</th>
</tr>
</thead>
<tbody>
<tr>
<td>Visits for depression</td>
<td>10.9% to 11.3%</td>
<td>4.2% to 5.5%</td>
<td>4.8% to 8.3%</td>
</tr>
<tr>
<td>Visit for antidepressants</td>
<td>6.5% to 7.7%</td>
<td>2.6% to 3.6%</td>
<td>3.0% to 6.2%</td>
</tr>
</tbody>
</table>

All increased; highest % increase for Hispanics; 1997 - Afr Am < Euro Am; Hisp NS
9. Garb: may relate to race differences/bias in schizophrenia vs diagnosis of mood disorders

10. Discussion: other possibilities??

B. Gender Differences in Depression:

1. Epidemiology:
      1) major dep: 2:1 to 4:1
      2) increased dysthyemia, SAD, minor dep
   b) gender difference emerges in adolescence, decreases in older age

2. APA Task Force Report: Women and Depression (McGrath et al., 1990); Sprock & Yoder (1997)
   update:
   a) Biological: lack of evidence for PMS, hormones, postpartum, menopause, BC pills
   b) Psychological
      1) learned helplessness/hopelessness model
      2) expression of emotions/ help seeking
      3) anger turned inward/depressive personality
      4) cognition: Nolan-Hoeksema: women ruminate, talk to friends (increases dep), men use
distraction (activity)
      5) roles: multiple roles may reduce dep in women
      6) social support: Veiel (1993): detrimental effects kin support networks on women
      7) socioeconomic plus crime, abuse

   a. review of epidemiology: confirms findings of gender diffs across cultures; some differences in cultures
   b. explanations: artefacts, genetics, diffs in anxiety or personality traits not supported
   c. support mixed for role of sex hormones and diffs in HPA axis; support for diffs in cognitive style,
gender roles, sexual abuse

   a. under-diagnosis due to gender specific manifestations of sx - more externalizing behs;
   b. Need to consider diff presenting sx, assessment, approach to tx
C. Gender Differences in Bipolar: Nair et al. (2000)

   a) no differences prevalence bipolar, women more severe depression, less severe mania
   b) women more likely bipolar II

2. Tondo & Baldessarini (1998) study and lit review: women only slightly more likely rapid cycling:
   (29.6% vs 16.5%) and results inconsistent

3. Nair et al. (2000): ANGIE
   a) women more likely rapid cycling, bipolar II, mixed states
   b) women more likely have dep episode onset (men onset of mania), more dep episodes
   c) unclear effects of hormonal factors
   d) special considerations using meds with women

D. Age

1. clinician bias: Perlick & Atkins (1984): increased dx of dementia vs dep in elderly pt, esp oldest old

2. depression, dementia and pseudodementia (APA Guidelines major dep, 2000): how differentiate??
   a. onset of sx? Which first? C/os vs minimizing; resp to meds; chronic dep can -> permanent cog decline

3. Newmann et al. (1991) different sx in older women?

4. Lebowitz et al. (1997): NIH Consensus Panel of Dx and Tx of Dep in Late Life
   a. different sx of depression in older adults: late onset dep more chronic, predicts Alzheimers or vascular dementia?

   b. treatment with medications or psychotherapy: less resp SSRIs, better resp TCAs but side effects; possibly slower response to CBT

   c. under-recognition of depression in the elderly: dep mood less prominent than neuroveg sx, may think dep normal in elderly; increased risk suicide

5. Cole & Dendukuri (2003): Risk factors for depression in the elderly:
   a. depression serious problem in elderly, up to 20% not identified

   b. identification of risk factors might help in screening of elderly for depression

   c. review and meta-analysis of 20 community studies

   d. found that bereavement (contrary to ECA study which found rare cause of depression in elderly), sleep disturbance, disability, hx of depression, female

6. Cook et al. (2004): tripartite model of depression and anxiety in the elderly: BRANDY
   a. quite a bit of research on depression, but little study of anxiety in elderly

   b. found support for 3 factor model of depression and anxiety in elderly; but need consider age-related differences
IV. Etiology and Treatment

Reading: Kendler et al. (2002); Tsuchiya et al. (2003); Klein & Santiago (2003); APA Practice Guidelines - Major depression and Bipolar; DeRubeis et al. (1999); Beutler (2000); Scott (2001)

A. Biological Theories:
   1. Genetic
      a) Family studies: bipolarI>bipolar II>unipolar dep
         1) Kraepelin recognized
         2) Andreasen et al. (1987): bipolar fam hx both bipolar & unipolar, unipolar fam hx dep only
         3) Gershon et al. (1982): study of 1254 relatives of probands

            Family rates of major depression when proband was diagnosed with:

            | Schizoaffective | Bipolar I | Bipolar II | Unipolar | Normal |
            | (N=11)         | (N=90)    | (N=34)     | (N=30)   | (N=30): |
            | Family rate major depression |
            | 37%           | 24%       | 25%        | 20%      | 7%      |

            Continuum model of genetic vulnerability from schizoaffective to bipolar to unipolar

      b) Twin studies: Rosenthal (1970) review:
         Concordance rates for unipolar and bipolar mood disorders in identical (monozygotic - MZ)
         and fraternal (dizygotic - DZ) twins:

         | MZ | DZ |
         | 40%| 10%|
         | 70-100%| 15-25%|

   2. Biochemical (see Table 1):
      a) indirect evidence-drug response; lab tests precursors, metabolites; receptors post-mortem

Table 1: Biochemical Theories of Mood Disorders:

<table>
<thead>
<tr>
<th>Depression</th>
<th>Mania</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Norepinehrine (NE): - Schildkraut (1965)</td>
<td>low NE</td>
</tr>
<tr>
<td>2. Serotonin (5- hydroxytryptamine: 5-HT) - Prange 1970s</td>
<td>low 5-HT</td>
</tr>
<tr>
<td>3. Permissive theory (NE &amp; 5-HT) Prange, lower 5-HT dampens NE signaling</td>
<td>low 5-HT AND low NE</td>
</tr>
<tr>
<td>4. Two Disease theory of depression: (one NE, one 5-HT)</td>
<td>Low NE OR Low 5-HT</td>
</tr>
<tr>
<td>5. Dopamine (DA) theory (mania) Bunney et al. (1979)</td>
<td>–</td>
</tr>
</tbody>
</table>

3. Structural and Other Biological Theories
   a) Akiskal & McKinney (1975): "final common pathway" of dep: abnormality in diencephalon
       (thalamus, hypothalamus): regulate emotions, arousal; really an interactive theory in which biol
       (genetic, neurotransmitters, other) factors + environment (psych, social, biol) ->
       depression

   b) electrolyte disturbance (mania) -> altered arousal

   c) biological rhythms (Johnson & Roberts, 1995): due to neurotransmitters, other biological, or
       environment, social -> dysregulation of rhythms and neuroveg sx

   d) redistribution of sodium (mania): abnormal distribution of sodium in sodium pump -> neuron
       Hyperexcitability (need balance potassium and sodium in neuron cell)

   e) Post: kindling and abnormal electrical discharges (mania, rapid cycling) (Johnson & Roberts,
       1995)

   f) endocrine dysfunction:
      1> thyroid: Hoggarty et al. (1993); Parry (1989): esp hypothyroidism in dep, women

      2> hypothalamus-pituitary-adrenalin (HPA) axis and Hypothalamus-pituitary-gonadal (HPG)
          axis in bipolar, rapid cycling, mixed states

      a] main problem is increased release of corticotropin releasing hormone (CRH) in neurons of the
         hypothalamus;
      b] however, recognizes is interactive: genetic factors result in lower norepinephrine, 5-HT or both,
         increase response of the HPA to stress - interacts with life events

4. Theories all recognize interaction of one or more biological factors with environmental factors

B. Biological Treatment

1. Medication (see Tables 2 & 3)
   a) Depression

      1) tricyclic and other cyclic antidepressants (TCAs): 1st line in past, 70% major dep respond to;
         a> Inhibit reuptake NE or 5-HT or both
         b> 4-6 wks at therapeutic level, no response -> switch another type or class
         c> side effects: anticholinergic, CNS, potentiate drugs, alc, mania (10% of bipolar pts), psychosis in
            schizoaffective, psychotic prone
         d> maintain full dose 6 mos after remission of sx; (1-2 yrs??); keep at full dose
2) selective serotonin reuptake inhibitors (SSRIs):
   a> newer, fewer side effects; inhibit reuptake of 5-HT;
   b> replaced TCAs as first line of defense (although new class of NRIs may equal in future??)
   c> consistent with 5-HT theory of depression
   d> used with other conditions (anxiety, personality dis, chronic pain, migraines, etc)

3) monoamine oxidase inhibitors (MAOIs)
   a> older, 2nd line today; for TCA, SSRI nonresponders, atypical dep and dep with anxiety,
      also pers dis (Bord pd) + dep; supposedly equally effective, possibly slower action
   b> similar to amphetamines
   c> tyramine restricted diets (MAO renders tyramine inactive, if inhibit, foods with tyramine
      have negative effects, high BP;

4) adjunctive medications: augment antidepressants
   a> lithium: helps 50% nonresponders
   b> seizure meds (tegretol, valproic acid)
   c> multiple antideps: TCAs + MAOIs, multiple TCAs, add thyroid hormones

b) Mania (medications)
   1) lithium carbonate:
      a> replaces intracellular sodium, stabilizes cell membrane
      b> short half life, 5-10 days to work, antipsychotics until then
      c> compliance a problem due to side effects (GI, weight, EPS, even TD, also renal,
         possible hypothyroidism) and pts’ enjoyment of manic state, fear of developing depression
   2) antipsychotics: calm before lithium works; to augment effects; for psychotic, noncompliant pts
   3) seizure meds: carbamazepine (tegretol), valproate:
      a> 2nd line of defense; nonresponders, rapid cycling; comorbid with BPD; pts who can’t
take lithium; 40% lithium resistant pts respond
b> kindling theory of bipolar and rapid cycling
c> used alone or to augment lithium;
d> caution: aplastic anemia with tegretol
e> valproate: agranulocytosis (depression bone marrow), polycystic ovaries for women

4) benzodiazepines: lorazepam, clonazepam: to augment; sedative, anti-seizure, anti-mania; abuse

2. ECT: severe dep, 78% effective, mania: 60-90% effective, good with catatonic features, older cardiac and medical problems (except aneurism, recent MI), pregnant, suicidal
   a) anesthetic + muscle relax, unilateral nondominant hemisphere (bilateral stronger, memory prob more likely)
   b) every 2 or 3 days or daily; 5-7 or 8-15 sessions
   c) possible autobiographical memory problems; relapse a problem
   d) controversies and pros and cons of use of ECT

3. Light Therapy: SAD, few side effects, questions remain: intensity, duration, timing, type of light (i.e., full spectrum); headaches, irritability, eye strain (Sato, 1997)
Table 2. Antidepressants and their mechanisms of action

I. Cyclic Antidepressants - reuptake inhibitors of norepinephrine (NE), serotonin (5-HT) or both

A. Tricyclics
   1. Imipramine (Tofranil)       NE = 5-HT
   2. Amitriptyline (Elavil)       5-HT > NE
   3. Desipramine (Norpramine)     NE
   4. Nortriptyline (Pamelor) - active metabolite of amitriptyline
   5. Doxepin (Sinequan)

B. Second generation amines
   1. Trazodone (Desyrel)          5-HT

C. Tetracyclics
   1. Amoxapine (Ascendin)         NE > 5-HT
   2. Also: Maprotiline HCL (Ludiomil)

II. Selective Serotonin Reuptake Inhibitors (SSRIs) - increase serotonin (5-HT) by inhibiting reuptake - all affect 5-HT; newer

A. Fluoxetine (Prozac): first - since 1988; potent, few side effects, can increase anxiety, long half-life, not use w/ MAOIs
B. Sertraline (Zoloft): since 1992; faster, fewer side effects (some GI), not use w/ MAOIs, claims stronger than prozac
C. Paroxetine (Paxil): since 1993; shorter half-life, no active metabolites, fewer side effects, may reduce anxiety, claims stronger than zoloft
D. Fluvoxamine (Luvox): newest - since 1995

III. Atypical Antidepressants - newer

A. Bupropion (Wellbutrin)-inhibits NE reuptake (& dopamine): 1989; increased risk seizures, agitation, fewer others
B. Nefazodone (Serzone)-5-HT agonist and reuptake inhibitor: 1995
C. Venlafaxine (Effexor)-bicyclic, 5-HT and NE reuptake (& DA): 1994
D. Mirtazapine (Remeron)-tetracyclic, increases 5-HT and NE: 1996

IV. Selective Norepinephrine Reuptake Inhibitors (NRIs) - increase norepinephrine (NE) by inhibiting reuptake: Reboxetine: new

V. Monoamine oxidase inhibitors (MAOIs) - increase NE by inhibiting monoamine oxidase (enzyme that metabolizes NE)
   A. Phenelzine (Nardil)
   B. Tranylcypromine (Parnate)

VI. Short acting Benzodiazepines
   A. Alprazolam (Xanax) Gamma Aminobutyric Acid (GABA)

Table 3. Antimanic medications and uses.

1. Lithium Carbonate                     Stabilizes cell membrane of neurons to reduce and prevent mania
2. Antipsychotics                       Reduce agitation; Reduce psychosis
3. Seizure medications
   a) Carbamazepine (Tegretol)           Lithium resistant bipolar and rapid cycling; use alone or with lithium
   b) Valproate, valproic acid
4. Benzodiazepines
   a) Lorazepam                           Calm, use lower level of lithium
   b) Clonazepam
B. Psychological Theories (mostly depression)

1. Psychoanalytic:
   a. Freud (1917) *Mourning and Melancholia*: original theory and revisions:
      1) anger against caretaker due to frustration, can’t express, turned inward
      2) loss of loved object; Harlows (1969) study with monkeys separated from birth; Spitz (1946) studies babies in orphanage separated 6-12 mos-> anaclitic depression
      3) loss -> depression if object loved ambivalently
      4) depression from greater than average number of losses

   b. O'Connell & Mayo (1988) review:
      1) Harris & Lloyd: death of parent early age assoc depression
      2) Paykel: low r between parental death and later dep
      3) Roy: parental death: increased rsik dep and other psychopath

2. Behavioral and cognitive:
   a. Lewinsohn Life Events theory (1947): low positive contingent reinforcement: poor social skills results in few positive reinforcements
      1) O'Connell & Mayo (1988): variable support
      2) Paykel: dep 3xs> neg life events, assoc with nonendogenous dep, 1st onset dep
      3) Johnson & Roberts: problem with research: retrospective studies, Q how measure life events

   b. Seligman Learned Helplessness theory: no control over negative life events -> helplessness, hopelessness and:
      1) internalization of failure: attribute neg to self
      2) externalization of success: attribute positive to luck, external, environment

   c. Beck's cognitive theory (1963): orig psychoanalytic therapist, recog p’s unreasonable thoughts
      1) maladaptive cognitions

      2) automatic thoughts

      3) negative cognitive triad: neg view of self, world, experiences

   d. Combined theories: cognitive diathesis interacts with stress: reformulated cog, learned helplessness
      1) negative cognitions interact with life events: cog diathesis (cog triad, learned helplessness) + neg stressors, life events; need to be consistency between area of vulnerability and type of life events; loss events more likely assoc with dep


      b) Simons et al (1993): cog factors (neg attitude) can generate neg life events in dep pts -> more dep; dep pts cause neg events (or could be dep pts report more neg life events);

      c) Hammen (1985; 1991) vulnerability model - interacts w/ negative life events: stress effects development of dep but dep causes neg life events, esp interpersonal (cycle)

      2) hopelessness depression and life events interact: learned hopelessness + life events interact in hopelessness type of dep

      a) Abramson et al (1988): hopelessness type of dep: assign stable, global causes to neg life events
b) Spangler et al (1993): relationship between hopelessness attributions and stressors; may be subset of pts with hopelessness type of dep

3) Life events interact with Biological vulnerability in bipolar disorder: Johnson & Roberts (1995): one of few psychological theories of bipolar, mania; biological components

   a) stress interacts with biological vulnerability due to several possible factors to influence course of the disorder
   b) circadian rhythms
   c) biobehavioral dysregulation: dysregulation in behavioral engagement system→ sensitivity to environmental events and more difficulty recovering from stress
   d) behavioral sensitization and kindling

4) Tsuchiya et al. (2003): risk factors for bipolar disorder: review of literature
   a) many inconsistent findings
   b) only family hx bipolar disorder has strong support
   c) some support for role of childbirth (increased risk for 3 mos after)
   d) suggestive role of season of birth, obstetric complications, stressful life events, brain injury, MS

D. Psychological Treatment (primarily depression)

1. Psychoanalysis and psychodynamic (including short term dynamic)
   a. description: free assoc, fostering transference, work thru early deprivation, loss, long term, 2-3/wk
      Recent briefer, insight oriented approaches
   b. efficacy: less evidence

2. Behavioral and cognitive (Jacobson et al., 1996): compared coping vs beh activation in CBT
   a. Both: time limited; focus on present: e.g., Beck’s: 15-25 sessions, 1/wk, severe dep: 2/wk 4-5 wks, then 1/wk 10-15 wks, booster sessions: 3-4/yr; identification maladaptive thoughts, replace w/ adaptive thoughts
   b. specific techniques: see Appendix 1

1) Life events theory (Lewinsohn): address social skills deficits that→ few positive reinforcements
   a) graded task assignment: activate
   b) social skills training
   c) relaxation training: reduce anxiety that interferes
   d) daily mood monitoring: assessment, also reactive effects

2) Learned helplessness theory (Seligman)
   a) alter environmental contingencies: to increase + events, reduce neg events
   b) set realistic goals
   c) social skills/assertiveness training: increase + outcomes of behavior

3) all include cog aspects, challenging negative attributions

4) Cognitive (Beck): mild-mod dep, adults, 1/wk; severe dep 2/wk 4-5 wks, then 1/wk 10-15 wks
   a) Behavioral: activate: start w/ esp more depressed
      1> activity assignments
      2> mood ratings; mastery & pleasure ratings
      3> social skills or relaxation training
b) Cognitive: next phase (or start w/ for less dep)
   1> identification (teach recognize, monitor); 3 column sheet
   2> challenge (Socratic dialogue, behavioral experiments);
   3> replace with rational cognitions

c) Collaborative empiricism- work w/ pt, educate on theory, automatic thoughts

5) See Appendix 2: CBT for depression:
   2A: behavioral techniques
   2B: cognitive techniques
   2C: cognitive distortions
   2D: five-column thought record

c. Efficacy of cognitive-behavioral txs
   1) Kovacs (1979): meds vs cog th vs beh th: 1/3 meds drop out; cog and social skills> meds
   2) Becker et al. (1987): social skills training, psychodynamic th, tricyclics: all equal for major dep
   3) Jacobsen et al., 1996: component analysis of cog th; compared beh activation vs beh
      activation + cog coping strategies( automatic thoughts, global schemas): no difference on
      followup

3. CBT for bipolar disorder as adjunct to medications: Scott (2001): support for the efficacy of CBT with bipolar

4. Interpersonal therapy (Klerman): Appendix 3
   a. Overview of procedures: dynamic and behavioral
      1) Identification of 1 of 4 interpersonal problem areas - Interpersonal Inventory:
         a) Grief, mourning, losses
         b) Role conflicts and disputes
         c) Role transitions (sometimes combined with b)
         d) Social isolation (sometimes combined with c)
         e) Deficits in social skills (last resort)
      2) Time limited (16-20 sessions or 12 sessions 1/wk then 1/mo maintenance); manualized
      3) Here and now, but insight oriented
      4) Keep focused on 1 primary interpersonal problem
      5) medical model, often combined with meds
      6) Appendix 3A: structural outline for IPT
      7) Appendix 3B: Goals and tasks of IPT
   b. Effectiveness IPT: 60% effective, up to 80-90% with meds
      1) Kupfer et al (1989): 63% recover 16 wks IPT + meds
      2) Elkin et al. (1989): large scale study; IPT=CBT=meds
      3) Klerman: 84% improve with IPT + TCAs, no recurrence 1 yr later

5. Effectiveness of psychotherapy vs medications: DeRubeis et al (1999):
   a. DeRubeis et al (1999): found CBT at least as effective as meds for severe major depression
   b. Antonuccio et al. (1995): Qs assumption that meds better than therapy or that meds+ therapy better
      than therapy alone: found that increasing pleasurable acts, changing maldaptive cogs, improving
      social skills as effective as meds
   c. Therapy may improve effectiveness of meds but meds not increase effectiveness of therapy: side
      effects meds can interfere with therapy
5. Selection between therapies, between meds and therapy:

   1) good prognosis assoc with good social support, low impairment, low chronicity/complexity, and if pt’s emotional stress is moderate (not too high or too low)
   2) meds: best response for pts with high impairment, high chronicity/complexity
   3) chronicity/complexity: multiperson therapy often best
   4) expose person to emotions or behaviors that are avoided
   5) start with focus on sx, sc reduction techniques
   6) externalizing pts: focus on skill building, sx removal
   7) internalizing pts: focus on insight, relationship
   8) avoid resistance: directiveness of the tx should be inversely related to pt’s resistance (or use a paradoxical approach in which sx are authoritatively prescribed)

b. Ablon & Jones (1999): compared IPT and CBT in tx of depression, NIMH Tx of Depression Collaborative Research Program:
   1) found similar outcome both approaches
   2) found a number of nonspecific factors common to both that were assoc with outcome (therapeutic alliance); also a number of differences
   3) need look at tx response in context of therapy – means across pt-therapist pairs findings; need more single-subject designs

6. Other Psychological Treatments:
   a. family therapy, marital, stress innoulation, problem solving, supportive (some evidence adds to effect meds) for depression
   b. mania, bipolar: not much literature;
      1) initially: structured environment, reality testing (like schiz)
      2) later: numerous issues: marital, family, individual, psychoeducation, prob solving, relapse prevention and early recognition, compliance with meds, likely many therapies for depression
   c. Discussion: Given so many options, how do you decide which ones to use (APA Guidelines- charts)