Bipolar Disorder

Background

1. Definition
   - Mood disorder defined by 1 or more episodes of mood elevation
     - Often characterized by frequent depressive Sx
   - Bipolar I Disorder
     - Episodes of sustained mania often with depressive episodes
   - Bipolar II Disorder
     - At least 1 major depressive episode and at least 1 hypomanic episode
2. General info
   - May initially present with depression in primary care setting; many are misdiagnosed
   - Prognosis for BD is worse, and tx is different than that for unipolar depression
   - Pts who present with depression should be asked specific questions to assess hx of mania or hypomania
   - Pts with BD more likely to have a family hx of BD and earlier onset

Pathophysiology

1. Pathology of disease
   - No dominant theory, although a genetic basis has been explored
   - Most studies have looked at neurotransmitter systems targeted by most effective therapeutic drugs
   - Some evidence for involvement of tryptophan hydroxylase 2 (TPH2) gene, which codes for rate limiting enzyme in synthesis of serotonin
2. Incidence/prevalence
   - Lifetime prevalence in United States 1-2.1%
     - True prevalence uncertain
       - Many BD pts may be undiagnosed or misdiagnosed with depression
   - Age of onset generally before 25 yrs
   - Bipolar I affects men and women equally
   - Bipolar II more common in women
3. Risk factors
   - 2 most important risk factors
     - Genetics/family hx
     - Personal hx
   - Studies of families have shown:
     - 40-70% lifetime risk for a monozygotic twin
     - 5-10% for a 1st degree relative
     - 0.5-1.5% for an unrelated individual
   - Another study showed that pts hospitalized for depression are at higher lifetime risk for BD
4. Morbidity/mortality
   - 25-50% of BD pts attempt suicide at least once
   - 15% actually commit suicide which is higher than rate for pts with depression and 30x rate in general population
   - 90% of pts with one manic episode will have future episodes

- 90% of BD pts will have at least 1 psychiatric hospitalization and two-thirds have 2 or more in their lifetime
- High rates of alcohol and substance abuse and anxiety disorder among BD pts contribute to morbidity

Diagnostics

1. History
   - Majority of BD pts will present with depression
   - 1st manic episode usually occurs 6-8 yrs after 1st depressive episode and may be brought on by stressful events
   - **Symptoms of mania:**
     - Elevated mood (or markedly irritable)
     - Inflated self esteem or grandiosity
     - Flight of ideas/racing thoughts
     - Rapid pressured speech
     - Increase in goal directed activity or psychomotor agitation
     - Decreased need for sleep
     - Mood congruent delusions
     - Distractibility
     - High risk behavior
       - Spending sprees, gambling, promiscuity
   - **DIGFAST**
     - Mnemonic representing Sx of manic episode:
       - **D**istractible
       - **I**rritable
       - **G**randiose
       - **F**light of ideas
       - **A**ctivity (incr)
       - **S**leep (decr need)
       - **T**alkative
   - May present with psychotic features making dx difficult
   - Primary symptoms, unlike those of schizophrenia, include disturbances in:
     - Sleep
     - Appetite
     - Activity level
   - **Signs of mania:**
     - Flamboyant dress
     - Socially inappropriate behavior
       - Grabbing others, masturbating
     - Flirtatious
     - Hyper-religious
     - Litigious
   - Other pertinent areas of hx
     - Personal hx of depression or substance abuse
     - Family hx of BD
     - Social hx indicating any of the above signs

2. Physical
    - Findings include any of above signs as well as assaultive or threatening behavior
3. Diagnostic testing
    - Functioning Assessment Short Test (FAST)
        - Short interview that scores impairment or disability and is useful for distinguishing euthymic pts from acute BD pts
    - Mood Disorder Questionnaire (MDQ)
        - 73% sensitivity, 90% specificity for BD with screening score >7, using structured clinical interviews for DSM-IV as reference standard
    - No useful screening test for BD in children
        - Refer to child psychiatrist
    - Full work-up should include:
        - TSH
        - CBC
        - Chemistries
        - Urine toxicities for substance abuse
    - Children
        - No well-validated screening instrument for dx of bipolar disorder in children exists
        - Kiddie Schedule for Affective Disorders and Schizophrenia (KSADS) with clinical evaluation by a childhood mental health specialist is used most often in major research studies
4. Diagnostic criteria
    - American Psychiatric Association
        - Defines episode of mania as a distinct period of abnormally elevated, expansive, or irritable mood lasting at least 1 wk (or any length if hospitalization is necessary) with $\geq$3 of the following:
            - Inflated self esteem or grandiosity
            - Decreased need for sleep
            - More talkative than usual
            - Racing thoughts or flight of ideas
            - Distractibility
            - Increase in goal directed activity
            - Excessive involvement in pleasurable activities that may have painful consequences such as spending money or sexual indiscretion
    - Hypomania
        - Defined by briefer duration ($\geq$4 days) of less severe manic Sx
        - Does not include psychotic Sx or require hospitalization
        - May result in improved functioning

Differential Diagnosis

1. Drug induced
    - Antidepressants
    - Glucocorticoids
    - ACTH
    - L-Dopa
    - INH

- PCP
- Psychostimulants
- Cyclobenzaprine (Flexeril)

2. Endocrinologic
   - Hyperthyroidism
   - Cushing's
   - Addison's
3. Neurological disorders
   - MS
   - Wilson's dz
   - Huntington's dz
   - Temporal lobe lesions
4. Other psychiatric disorders
   - Personality disorders
   - Schizophrenic disorders
   - PTSD
5. Consider toxicity 2° to mood stabilizing meds
   - Lithium, Depakote, Tegretol
6. Assess for ETOH, drug withdrawal / intoxication:
   - Cocaine, PCP, speed, hallucinogens
7. Consider dx that mimic, cause or exacerbate mood disorders:
   - Hyperthyroidism
   - Delirium
   - CNS infection
   - SLE
   - CVA
   - HIV
   - 3° syphilis

Therapeutics

1. Acute treatment
   - Mood stabilizers
     - Lithium
     - Valproate
     - Carbamazepine
   - Antipsychotics may also be used alone or with a mood stabilizer:
     - Olanzapine
     - Risperidone
     - Quetiapine
   - Benzodiazepines
     - May also be used in addition to mood stabilizers
   - Also consider anticonvulsants, psychotherapy, ECT, and referral to a psychiatrist / psychologist
2. Further management (24 hrs)
   - Mania: maintenance Tx
     - Antipsychotic with lithium or valproate to reduce recurrence of manic episodes
     - Pregnancy

        - Lithium 1st line treatment
        - Monotherapy preferred for women of childbearing age
    - Depression: maintenance Tx
        - Lithium
        - Lamotrigine
            - Beneficial for both acute treatment of bipolar depression and prevention of recurrent episodes
    - For patients who do not respond to 1st line Tx, consider adding a 2nd mood stabilizer or atypical antipsychotic
    - Critical complications include:
        - Signs and symptoms of a hypomanic / manic episode often signaled by decrease in sleep
3. Long-term care
    - Lifelong Tx for pts who experience 1 severe manic episode to 3 or more manic episodes
    - Treatment of choice:
        - Mood stabilizers, esplithium which is effective against depression and when administered long-term has been shown to reduce risk of suicide based on a systematic review of randomized trials
    - Fully integrated care includes psychotherapy and Tx of substance abuse and anxiety disorders

Follow-Up

1. Return to office
    - Time to follow-up is based on clinician's judgment, new Tx prescribed, and severity of Sx
    - For pts initiating lithium, labs should be checked in 5 days to assess steady state level and regularly monitored thereafter
    - Pregnancy
        - When prescribing lithium or anticonvulsants (valproic acid, carbamazepine), draw blood levels monthly during 1st and 2nd trimesters, and then weekly in 3rd trimester
2. Refer to specialist
    - Psychiatrist / psychologist consult based on severity of Sx, provider comfort with condition, and response to standard Tx
3. Admit to hospital
    - Consider hospitalization
        - Pts who pose a danger to themselves or others
        - Pts who are unable to care for themselves
        - Pts with elevated mood stabilizing drug levels
        - Pts with concurrent medical problems
        - Pts with multiple recent visits to ED
    - Be cautious & reluctant to discontinue manic pts, esp if 1st episode
    - Do NOT let unstable manic pts sign out AMA, admit involuntarily
    - If pt judged able to comply without patient care, discharge with follow up may be practical and safe

- If pt stable for discharge, in outpatient tx & has become noncompliant with meds, offer same medication with several days' worth to discharge and follow up with outpatient psychiatric care

Prognosis

1. Even with remission, most pts who have 1 episode of mania will have recurrences
2. Significant suicide risk
   - Hospitalization is often required
3. Most pts can expect lifelong pharmacotherapy to reduce occurrence of mania / depression and reduce risk of suicide

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Evidence-Based Inquiry

1. What's the best strategy for bipolar disorder during pregnancy?
2. Which tool is most useful in diagnosing bipolar disorder in children?
3. What drugs are best for bipolar depression?

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