Mood (s. Affective) Disorders

Etiopathogenesis

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2. Other biologic factors

3. Psychological and social factors

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2. Manic episode
3. Mixed episode
4. Hypomanic episode

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EPIDEMIOLOGY

TREATMENT

EPIDEMIOLOGY

TREATMENT

EPIDEMIOLOGY

TREATMENT

EPIDEMIOLOGY

TREATMENT

SEASONAL AFFECTIVE DISORDER (SAD)

Mood (s. Affective) Disorders - disturbance of mood along happy-sad axis.

Two basic mood abnormalities, depression and mania, occur on continuum from normal to clearly pathological. While minor symptoms may be extension of normal sadness or elation, more severe symptoms are associated with discrete syndromes (affective disorders) that differ qualitatively from normal processes. Depression is morbid sadness, dejection, or melancholy, whereas mania is disordered mental state of extreme excitement. Both have accompanying emotional - cognitive - motoric features.

• overly intense, continue longer than expected for causative event, occur without cause + impaired function!

ETIOPATHOGENESIS

- Interaction of GENETIC, BIOLOGIC and PSYCHOSOCIAL factors determines which individuals will develop mood disorders.

Historical concept - EXOGENOUS-ENDOGENOUS DICHOTOMY - endogenous depression (caused by biologic factors) and exogenous depression (caused by loss or other environmental stresses)

ETIOLOGY

- over years, experts have debated whether mood disorders represented brain disease or reflected intrapsychic conflicts; recently, they have returned to belief that conditions represent multifactorial biologic process.

GENETIC FACTORS

- mood disorders run in families - mood disorders are at least partly genetic.

- no single chromosomal site seems to play dominant role (i.e. multiple different genetic loci, each of small effect).

- expanding triplet repeats may account for finding that bipolar illness has earlier onset and more severe symptomatology in subsequent generations of some families.

MAJOR DEPRESSIVE DISORDER

- 50% patients have 1st-degree relative with mood disorder (more often depression than bipolar).

- concordance for monozygotic twins = 50%, for siblings (including fraternal twins) = 15%.

- Bipolar disorder (higher genetic influence than in major depressive disorder?)

- 90% patients have 1st-degree relative with mood disorder (either bipolar or depressive).

- concordance for monozygotic twins = 33-90%, for siblings (including fraternal twins) = 5-25%.

- 1st-degree relatives of patient with BP I are 7 times more likely to develop BP I than general population.

Multiple vulnerability genes operate in different families by different mechanisms and through complex interactions with life events.

NEUROCHEMICAL FACTORS

- All clinically useful antidepressants potentiate, either directly or indirectly, actions of NOREPINEPHRINE, DOPAMINE, and/or SEROTONIN in brain → BIOGENIC AMINE THEORY.
depression is due to deficiency of biogenic amines at certain key sites in brain; vs. mania is caused by overproduction of these neurotransmitters.

Norepinephrine is associated with mood disorders:
- Some antidepressants (e.g. DESIPRAMINE, NORTRIPTYLINE) down-regulate noreceptors.
- NE metabolites are generally diminished in depression.
- Decreased NE activity has been speculated to be involved in mania.

Serotonin:
- Selective serotonin reuptake inhibitors are effective antidepressants.
- 5-HT depletors (e.g. by tryptophan-depleted diet) can worsen depression.
- Is less solidly linked to depression.

Dopamine:
- Is effective antidepressant that is dopaminergic without directly affecting 5-HT or NE transmission.
- Parkinson disease (dopaminergic dysfunction) often leads to depressive symptoms.

Other Biochemical Factors

Neuroendocrine regulation
- Hypothalamus-pituitary-adrenal axis in depression. In dexamethasone suppression test depressed patients exhibit nonsuppression (i.e. cortisol remains elevated after administration of dexamethasone).
- Hypothalamic lesions may mimic depression, and hypothyroidism may mimic mania.

Sleep and circadian rhythm
- Depressed patients experience insomnia or hypersomnia; manic patients typically have decreased need for sleep.
- In polysomnography many depressed patients have shortened rapid eye movement (REM) latency (i.e. time from falling asleep to first REM period is about 60 minutes rather than 90 minutes).
- Sleep deprivation is effective treatment for depression (although depression returns after next night's sleep).

Diagnosis:
- Requires identification of mood episode, which are not actual diagnoses in themselves (rather, they are building blocks clinicians use in making diagnosis of mood disorder).

N.B. if patient has ever had psychotic features (delusions or hallucinations) for at least 2 weeks in absence of mania or major depression, then psychotic disorder (rather than mood disorder with psychotic features) must be diagnosed.

N.B. if mood change is due to general medical condition or substance use other mood disorder diagnoses (e.g. major depressive disorder) are not made! e.g. 60-year-old woman on recently started steroid treatment and now has major depressive symptoms = mood disorder due to corticosteroid treatment, with major depressive-like episode.

1. MAJOR DEPRESSIVE EPISODE (MDE)
A. ≥ 5 of following symptoms have been present during same 2-week period and represent change from previous functioning (baseline); at least one of symptoms is either (1) depressed mood or (2) loss of interest/pleasure.

1. Depressed mood most of day, nearly every day, as indicated by either subjective report (e.g. feels intense sadness, hopeless) or observation made by others (e.g. appears tearful); in children and adolescents, irritable mood suffices.

2. Markedly diminished interest/pleasure (anhedonia) in all, or almost all, activities most of day, nearly every day (as indicated either by subjective account or observation made by others).

3. Weight loss/weight gain (≥ 5% of body weight in 1 month), or appetite disturbance.

4. Insomnia or hypersomnia nearly every day.

5. Psychomotor agitation/retardation nearly every day (observable by others, not merely subjective feelings of restlessness or being slowed down).

6. Energy or fatigue loss nearly every day.

7. Feelings of worthlessness or excessive/supernormal guilt (which may be delusional) nearly every day (not merely self-reproach or guilt about being sick).

Negative thinking (often with ruminative features) predominates!

8. Diminished ability to think/ concentrate, or indecisiveness, nearly every day (either by subjective account or as observed by others) or grossly impaired cognition

9. Recurrent thoughts of death (not just fear of dying); recurrent suicidal ideation (with or without specific plan; or suicide attempt).

B. Symptoms cause clinically significant distress or impairment in functioning (social, occupational or other important areas).

C. Symptoms are not due to direct effects of substance (e.g. drugs of abuse, medicaiton) or general medical condition (e.g. hypothyroidism).

D. Symptoms are not better accounted for by bereavement (after loss of loved one, symptoms persist for longer than 2 years) or characterized by marked functional impairment, morbid preoccupation with worthlessness, suicidal ideation, psychotic symptoms, or psychomotor retardation.

1. Major life stresses (esp. separations and losses) commonly precede MDE.
2. Attack gradually builds over period of week to month, and if untreated may last 3-8 months.
3. In primary care setting, presenting complaints often can be somatic (fatigue, headache, abdominal distress, change in weight).
some patients demonstrate mood congruent psychotic features (e.g. content of delusion or hallucination reflects depression). e.g. mood congruent delusion might be that one has committed terrible crimes or sins; mood congruent hallucination might be that one talks to dice or says that one is a loser.

depression can produce measurable cognitive deficits / worsening of pre-existing dementia (appears to arise from dopamine, serotonin, or glutamate dysfunction or neurotransmitter imbalance). Symptoms of depression (e.g. pseudodementia) - REMs with successful treatment of MDE.

Mood disorders due to general medical condition: Mood disorders with transient onset and remission due to general medical condition (e.g. hyperthyroidism). Mood disorders due to substance use: Mood disorders with permanent onset and remission due to substance use (e.g. alcohol, amphetamines).

Stress-induced mood disorder: a) Intoxication with depressant drugs (e.g. alcohol, opiates, barbiturates) b) Withdrawal from stimulants (e.g. caffeine, amphetamines)

c) Sleep disturbances (e.g. sleep apnea), encephalitis, HIV, neurosyphilis, tuberculosis, brain tumors (diencephal, temporal region). d) Disorders involving hypothalamic-pituitary-adrenal axis or thyroid (Cushing disease, hyperthyroidism). e) Other - pernicious anemia, pancreatitis, cancer, renal failure.

Normal forms of sadness - grief (normal emotional response to loss), bereavement (normal emotional response to death of a loved one).

Mood disturbance - at least 2 of the following symptoms have persisted (4 if mood is only irritable) and have been present to significant degree:

1. Inflated self-esteem or grandiosity (up to grandiose delusions); extreme self-confidence with impaired judgment.

2. Decreased need for sleep (e.g. feels rested after only 2-3 hours of sleep). 3. More talkative than usual or pressure to keep talking (pressured speech).

4. Flight of ideas or subjective experience that thoughts are racing.

5. Distractibility (i.e. attention too easily drawn to unimportant or irrelevant external stimuli) - demonstrated by vigilance tests (part of mental status exam).

6. Increase in goal-directed activity (e.g. socially, at work or school, or sexually) or psychomotor agitation.

7. Excessive involvement in pleasurable activities that have high potential for painful consequences (e.g. gambling, sexual promiscuity, reckless driving, unrestrained buying sprees, foolish business investments).

Mood disturbance - sufficient to cause marked impairment in occupational functioning or in usual social activities or relationships with others or to necessitate hospitalization to prevent harm to self or others, or there are psychotic features.

Elderly persons experience more somatic - cognitive symptoms (confusion with general decline in functioning) and fewer complaints of sad or dysphoric mood; of particular importance is increasing risk of suicide among elderly persons.

Children may present with misleading symptoms – marked irritability (!!!), decline in school performance, social withdrawal, somatic complaints (headaches, chest, abdominal, or back pains); children 7-18 months may demonstrate, ANIC EPISODE; cause is lengthy separation (1 > week) from caregivers with whom child has established attachment relationship; symptoms - listlessness, anorexia, psychomotor retardation, sad facial expression, sleep disturbance; restitution of relationships; preschool children often demonstrate behavioral difficulties (hyperactivity, aggression) - often a normal developmental遗迹. - schoolchildren already manifest usual signs and symptoms of depression.

Mood disorders due to general medical condition:

1. Neurological disorders - stroke (particularity of left frontal lobe), seizure disorders, MS, MELAS, Parkinson disease, sleep apnea, encephalitis, HIV, neurosyphilis, tuberculosis, brain tumors (diencephal, temporal region).

2. Disorders involving hypothalamic-pituitary-adrenal axis or thyroid (Cushing disease, hyperthyroidism).

3. Other - pernicious anemia, pancreatitis, cancer, renal failure.

Normal forms of sadness do not respond favorably to psychotherapy or antidepressants.

2. Manic episode

A. Distinct period of abnormally and persistently elevated, expansive, or irritable mood lasts at least 1 week (or any duration if hospitalization is necessary).

B. During period of mood disturbance, at least three of following symptoms have persisted: (4 if mood is only irritable) and have been present to significant degree:

1. Inflated self-esteem or grandiosity (up to grandiose delusions); extreme self-confidence with impaired judgment.

2. Decreased need for sleep (e.g. feels rested after only 2-3 hours of sleep).

3. More talkative than usual or pressure to keep talking (pressured speech).

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C. Mood disturbance - sufficient to cause marked impairment in occupational functioning or in usual social activities or relationships with others or to necessitate hospitalization to prevent harm to self or others, or there are psychotic features.

Note: manic episodes that are clearly precipitated by somatic antidepressant treatment (e.g. medication, electroconvulsive therapy, light therapy) should not count toward diagnosis of bipolar I disorder.

Manic episode usually develops over few days.

Patients often are too bright, colorful, or garish manic episode usually develops over few days.

Mood disturbance due to general medical condition (e.g. hyperthyroidism).

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Mood disorder due to general medical condition (AIDS, Cushing disease, hyperthyroidism, lupus, temporal lobe epilepsy, MS, Wilson disease, neurosyphilis).
4. HYPOMANIC EPISODE

- similar but less severe than manic episode:
  a. episode lasts ≥ 4-days.
  b. episode must not lead to hospitalization, must not include psychotic features (e.g. delusions), and must not cause severe social / occupational impairment.
- for some people, hypomanic states contribute to success in business, leadership, achievement, and artistic creativity; however, they more often have serious detrimental interpersonal and social results (e.g. interpersonal relationships are often stormy).

CLASSIFICATION

<table>
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<th>Disorder</th>
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<th>Milder Depression</th>
<th>Manic or Mixed Episode</th>
<th>Hypomania</th>
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<td>Cyclothymia</td>
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*+w = syndrome must be present to make diagnosis; *

- w = syndrome must be absent to make diagnosis; 
- w = this syndrome may be present or absent.

1. major depressive episode must not occur during first 2 years of illness. 
2. manic episode must not occur during first 2 years of illness.

DM-IV provides SPECIFIERS that better describe current (or most recent) mood episode:

1. Severity/remission status - mood episodes can be: mild / moderate / severe and in partial / full remission.
   *presence / absence of psychotic features should be noted (psychotic features should be described as mood-congruent or mood-miscongruent).

2. Catatonic features - when mood episode features two of following:
   a) immobility
   b) excess purposeless activity
   c) negativism or mutism
   d) posturing, mannerisms or stereotypic behaviors
   e) echolalia or echopraxia.

TREATMENT

- patients with mood disorders are most often treated in outpatient settings by clinicians other than mental health professionals.
- indications for voluntary or involuntary hospitalization:
  1) dangerous / disorganized patients
  2) failed outpatient treatment

N.B. mood disorders are often recurrent! - good follow-up care after acute episode is key to successful treatment!

MAJOR DEPRESSIVE DISORDER (MDD)

- presence of ≥ 1 major depressive episode* 
- absence of any manic, hypomanic, or mixed episodes.
- patients are at risk for other psychiatric conditions (e.g. alcohol in other substance abuse, anxiety disorders).

MELANCHOLIC (more severe subtype of major depression) - profound anhedonia + three of following:

a. distinct quality to sad mood (e.g. it does not resemble normal grief or sadness)

b. symptoms worse in morning

c. early morning awakening

d. marked psychomotor changes

e. marked anorexia / weight loss

f. excessive guilt

EPIDEMIOLOGY

- lifetime risk 20% for women, 12% for men (i.e. ≈ 15 times more common than bipolar disorder).

Primary care providers should strongly consider presence of depression in their patients!

Major depression is most common psychiatric disorder!!!

- risk factors:
  1) 1°-degree relatives with mood disorders. see above
  2) chronic medical illnesses, alcoholism, panic disorder, psychosocial stress* - there can play role in both initiation and maintenance of MDD.

*significant losses in early life predispose to MDD over lifespan of individual!

- point prevalence 2-4% for men, 4-6% for women.

- mean age of onset - mid 20s (range from preschool childhood to old age); rates are highest in 25-44 years.

- of teenagers diagnosed with MDD, bipolar disorder is diagnosed in 50% of them as they grow into adulthood.

DIAGNOSIS

Results of dexamethasone suppression test (DST) are positive if patient fails to suppress plasma cortisol levels to < 5 μg/dL between 8 and 24 hours after oral dose of 1 mg dexamethasone given at 11:00 P.M. night before.

- DST is not useful for diagnosis - false-negative rate = 50%.
- DST can be useful for monitoring treatment of patients who have abnormal DST response.

EEG - relative absence of slow-wave sleep (stages 3 and 4), shortened period between sleep onset and first dreaming period (REM latency), lengthened first REM episode & shortened first NREM episode

- these disturbances of sleep improve when mood disturbance improves.
TREATMENT

Thought content always should be assessed for suicidal/homicidal/violent ideation!

- physical activity & exercise contribute to recovery from MDD.
- REMISSION – minimal or no symptoms; RESPONSE - 50% reduction in symptoms.

PSYCHOTHERAPY

a) psychodynamic (psychoanalytically oriented) psychotherapy - most commonly used with depressed patients.

b) effective intensive brief forms of time-limited therapy - cognitive psychotherapy and interpersonal psychotherapy.

- patients are usually relieved when their suffering is recognized and they are permitted to discuss it.
- psychotherapy most effective once somatic and melancholic symptoms have improved with medication.
- long-term psychotherapy is unnecessary.

- support is important - family & friends, day hospitalization, supportive living arrangements (group homes).

MEDICATIONS

1. Antidepressants see p. 575 >>

SSRIs are first-line drugs for depression!

- Psychostimulants (DEXAMETHASONE, PREDNISONE, METHYLPREDNISOLONE) - augmenting agents in resistant depression (esp. patients who are medically ill).

2. Antipsychotic medications – for depression with psychotic features.

3. Thyroid hormones (LITHUIONE) - may convert nonresponders (to antidepressants) to responders by inducing serotonergic sensitivity and enhancing effects of TCAs.

- it is standard of care to initiate antidepressant at time of diagnosis.

- always ask how patient’s relatives with depression fared on different antidepressant drugs, because new patient will likely fare similarly.

- follow-up ambulatory visits should be scheduled on regular basis and more frequently than for other medical treatments; if improvement has not begun in 4–8 weeks → psychiatric consultation.

N.B. treatment failures often are caused not by clinical resistance, but by noncompliance/ inadequate duration of therapy/acute inadequate dosing!

- treatment duration:
  - once episode is resolved successfully, treatment should be continued for 6 months + 1 year (to prevent risk of relapse).
  - most antidepressants (esp. SSRIs) should be tapered off (by decreasing dose by ≈ 25%/week) rather than discontinued abruptly.
  - most experts now argue that children who have experienced ≥ 2 major depression episodes should be treated indefinitely.

TRANCRANIAL MAGNETIC STIMULATION

- Less effective but substantially safer than ECT

NEUROSTIMULATION (ELECTROCONVULSIVE THERAPY): - safe and effective treatment see p. 573 >>

- extremely effective in severe depression!!!

- more rapid onset of action than drug treatments.

- reserved for:
  a) those who have failed trials of antidepressants.
  b) depression with psychotic features.
  c) severe suicidal depression.
  d) depression during pregnancy.
  e) patients who have stopped eating.

- release after ECT is common, and drug therapy is often maintained after ECT.

- side effects - cognitive deterioration.

TRANCRANIAL MAGNETIC STIMULATION

- may have some efficacy as augmenting agent with antidepressant medication.

VAGUS NERVE STIMULATION

- investigational; some long-term efficacy in treatment-resistant depression.

DBS

- up to 20% patients are refractory to standard therapies – niche for DBS.

- DBS for depression remains in research phase.

Targets:

1. subcallosal cingulate gyrus (s. subgenual cingulate gyrus, area Cg25) – the midpoint between the genu of corpus callosum and the anterior commissure – hypermetabolic in depression (and even in normally sad mood) and normalizes with successful treatment with antidepressants; only specific area is responsive to DBS (need DTI to find the confluence of bundles) – see studies below:

2. nucleus accumbens – promising target (old studies were targeting too high).

3. rostral cingulate cortex (area 24a)

4. ventral capsular/ventral striatum

5. inferior thalamic peduncle

6. lateral habenula

7. anterior limb of internal capsule

Studies

- subcallosal cingulate deep brain stimulation for treatment-resistant depression: a multisite, randomised, sham-controlled trial.

- Psychosurgery for depression with psychotic features: a multisite, randomised, sham-controlled trial.

- Multicenter randomized trial of subcallosal cingulate stimulator for treatment-resistant depression: a sham-controlled trial.
- all patients had been unresponsive to a minimum of four antidepressant medications from at least three drug classes. 
- average duration of depression prior to receiving DBS in the current study was 12 years. 
- DBS targeting bilateral subcallosal cingulate white matter. 
- Nucleus Xp Deep Brain Stimulation System (St. Jude Medical). 
- randomised to 6 months of active or sham DBS, followed by 6 months of open-label subcallosal cingulate DBS; at the conclusion of the 12-month study, a subset of patients were followed up for 4 to 24 months. 
- primary outcome was frequency of response (defined as ≥ 40% reduction in depression severity from baseline on Montgomery-Åsberg Depression Rating Scale) averaged over months 4 to 6 of the double-blind phase. 
- futility analysis was performed when 90 patients (approximately half of the proposed sample) received DBS implantation and completed the double-blind phase. 
- finding: 1) both groups showed improvement, but there was no statistically significant difference in response during the double-blind, sham-controlled phase (12 out of 60 [20%] patients in the stimulation group vs 5 out of 30 [17%] patients in the control group). 
- 2) 28 patients experienced 40 serious adverse events, 8 of these (in 7 patients) were deemed to be related to the study device or surgery. 
- 3) not all patients reached the follow-up endpoint; at 30-month follow-up, the antidepressant responses improved in 29% of patients at 12 months, 35% at 18 months, and 49% at 24 months; remission rates also improved, from 14% of patients at 12 months to 18% at 18 months and 26% at 24 months. 
- interpretation: 
  1) study confirmed the safety and feasibility of subcallosal cingulate DBS as a treatment for treatment-resistant depression 
  2) study did not show statistically significant antidepressant efficacy in a 6-month double-blind, sham-controlled trial. 6 additional months of DBS did not increase the proportion of patients who responded to DBS or who achieved remission. 
- long-term outcomes are clinically meaningful and greater than would be expected with treatment as usual in this highly treatment-refractory patient population," authors conclude that "the negative outcome of this trial should not be interpreted simply as a failure of subcallosal cingulate DBS for treatment-resistant depression." 


LITIM INNIT 

P R O G N O S I S 

- 50% patients experience recurrence (after two episodes, recurrence rate is ≥ 70%, and after three episodes = 90%). 
- some have relapses of sufficient frequency to warrant long-term preventive use of antidepressant medications (resistant patients can discontinue treatment after resolution of episode). 
- in addition to high risk of suicide (see below >>), patients have higher risk of illness / death due to medical causes (impaired food intake, alcoholism, drug abuse, own health neglect, etc). 
- depression increases risk of MI and stroke. 
- some patients may perform homicide! 

S U I C I D E 

- suicide is uniquely human behavior. 
- 11th cause of death in USA. 

Mood (S. Affective) Disorders 

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Etiologic Factors
Psychiatric illness is present in almost all people who commit suicide! concomitantly (i.e. multiple psychiatric illnesses) is common.

major risk factor — MDD (lifetime risk of suicide 2-15%)
   - MDD plays role in > 50% of all suicide attempts.
   - suicide risk is highest initially after hospital discharge (when treatment has been initiated and psychosocial activity is returning to normal but mood is still dark); risk remains high for 1 yr after discharge.

other factors that increase risk of suicide:
1) alcohol use (plays role in > 25% suicides), substance use
   - Alcohol / drugs of abuse increase disinhibition and impulsivity = worse mood!
   - Alcoholics are suicide-prone even when sober!
2) schizophrenia (5% suicides)
   N.B. schizophrenia has = same risk for suicide as major depression!!! (i.e. = 10% schizophrenia attempt suicide)

3) delirium, dementia, and other cognitive disorders (4% suicides)
4) borderline and antisocial personality disorders
5) panic disorders
6) history of suicide attempts
7) family history of suicide (suicide runs in families!)
8) agitation or delusional ideas, command hallucinations
9) premenstrual state
10) personally significant anniversaries
11) social isolation (e.g. divorced, widowed, unemployed)
12)chronic painful medical illness or acute disabling change in physical health.
13) men > 55-69 yrs (elderly account for 10% American population and 25% suicides).
14) white race, some Native American groups
15)access to firearms

there appears to be genetic risk of suicide that is independent of risk of psychiatric illness (e.g. suicides occur only among monzygotic twins, not among dizygotic pairs).
suicide is less common among practicing members of most religious groups (particularly Roman Catholics)
power of suggestion - rise in suicides is seen after well-publicized suicide (e.g. of rock star) and among self-identified populations (e.g. high school, college dormitory).

Methods
method choice is determined by cultural factors, availability, seriousness of intent.
some methods (e.g. jumping from heights) make survival virtually impossible, whereas others (e.g. drug ingestion) make rescue possible.
N.B. using method that proves not to be fatal does not necessarily imply that intent was less serious.
bizarre method suggests underlying psychosis.
most frequent methods:
   - in suicide attempts - drug ingestion.
   - list completed suicides - firearms (74% men, 31% women), hanging (men), drug ingestion (women).

Clinical Presentation
Suicidal behavior includes:

I. Self-destructive acts
   a) completed suicide - results in death.
   b) attempted suicide - act intended to be self-lethal, but one that does not result in death (frequently, suicide attempts involve at least some ambivalence about wishing to die and may be cry for help).

25-200 attempts are made for every death, rate of attempts is disproportionately high among adolescent girls

II. Suicidal ideation - thoughts and plans about suicide.
   a) suicide gestures - attempts that involve action with very low lethal potential (e.g. inflicting superficial scratches on wrist, overdosing on vitamins).
   - in suicide attempts - drug ingestion.
   - list completed suicides - firearms (74% men, 31% women), hanging (men), drug ingestion (women).

III. Suicidal behavior - patient may ingest drugs, slash wrists, take overdose, jump out window → patient often requires medical / surgical intervention (gastric lavage, suturing, etc) before psychiatric assessment, patient is considered acutely suicidal until proven otherwise → careful observation to prevent patient from leaving ED (→ another suicide attempt).

Suicidal ideation - patient may be obviously depressed, expressing concerns with little distress out of proportion to objective findings or may visit ED many times over short period; patient may take medication given for somatic symptom and then commit suicide.

Suicidal behavior - although patient denies implications of her behavior, she may have accidents that range from surprisingly to obviously suicidal; special type - patient appears homicidal or assaultive but his behavior is primarily attempt to provoke others (such as police) to kill him!

Suicidal ideation - patient seeks medical evaluation for somatic symptom; patient may show distress out of proportion to objective findings or may visit ED many times over short period; patient may take medication given for somatic symptom in suicide attempt!

C. Chronic suicidal ideation and behavior - patient repeatedly calls or visits ED for suicidal ideation and attempts.
   - by self-destructive behavior patient attempts to manipulate environment or relieve internal destructive behavior patient attempts to manipulate environment or relieve internal
   - patient may say so much hostility that physician may wish that patient were dead (others in patient's environment may feel similarly!!!).
   - risk for suicide is greater by design, miscalculation, or impulsiveness.

Situations that must arise suspicion:
1. Unemployed divorced white men > 45 years.
2. Patient reports hopelessness, helplessness, loneliness, exhaustion.

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TREATMENT

- patient should not be left alone until he is in secure environment - 10% people who make attempt will eventually die by suicide (due to reattempt).
- psychiatric assessment ASAP for all patients
- transportation to psychiatric facility should be accompanied by trained professionals (e.g. ambulance, police), never by family members or friends
- availability and support of family and friends are crucial (they need to be interviewed away from patient to feel comfortable stating their concerns).
- patient should be hospitalized if lethality of ideation/behaviour is high (e.g. persistence of patient's wish to die, severity of concurrent psychopathology, absence of reliable sources of support in social environment, persistence of causative crisis in patient environment).
- features of high risk attempted suicide:
  1) hanging or gunshot (vs. overdose with OTC drugs, superficial cuts on wrists).
  2) attempt in isolated area (vs. highly visible location).
  3) suicide attempt if first episode is hypomanic or depressed, proper diagnosis will not be made until later emergence of mania.
  4) patient's perception of lethality of unsuccessful attempt, expectations of rescue, and relief or disappointment at being alive are often more important than objective dangerousness of attempt.
- severely suicidal patient who resists treatment may require one-on-one observation to prevent escape or self-injury.

- criteria for outpatient treatment:
  1) no psychosis
  2) no active suicidal ideation
  3) good social support
  4) low-risk suicide attempt

- communication with individual threatening imminent suicide (e.g. patient who calls and declares that he is going to take lethal dose of drug):
  - remind him of his identity (i.e. use his name repeatedly);
  - help sort out problem that has caused crisis;
  - offer constructive help with problem;
  - encourage to take positive action;
  - remind him that family and friends care for him and want to help.

- communication with individual about suicidal thoughts:
  - patient's perception of lethality of suicidal ideation/attempt;
  - no psychosis;
  - no active suicidal ideation;
  - no plan;
  - no means;
  - communication with trained professionals (e.g. family members, friends).
- directly related to phase of episode.
  - historically, treatment was attempted with *psychosurgery* (such as prefrontal lobotomy).
  - *ECT* is highly effective for both phases of illness (esp. in treatment-resistant cases).

**Mood MANIA** (hospitalization may be necessary; e.g. patient’s behaviors destroys his career and is harmful to those around them) Manic excitement is medical emergency - patient can die of exhaustion!

**A. Psychotherapy**, (accumulated stresses can propel person into mania or depression).

**B. Medications** (compliance is large problem – impaired judgment* + many patients prefer hypomania to euthymia): *once mania begins, patients believe that they know better than their physicians*

1. **LITHIUM** - effective for acute mania and for maintenance (relapse rates reduced 50%); dosage and blood level need to be higher during acute treatment than during maintenance prophylaxis. (e.g. PsY 15.5%)
2. **Anticonvulsants** (*CARBAMAZEPINE, VALPROATE, LAMOTRIGINE*) - used if lithium is ineffective or poorly tolerated:
   - effective alone or as adjunct to LITHIUM in acute treatment and/or maintenance (maintenance doses are similar to those used in seizure disorders).
   - especially effective in prevention of rapid mood swings.
   - VALPROATE is as effective as LITHIUM in acute mania (even more effective in mixed episodes).
   - mechanism of action - suppression of subseizure threshold electrical kindling activity in limbic system.
3. **Antipsychotic drugs** - symptomatic relief in acute mania while mood stabilizers are taking effect; long-acting antipsychotics (esp. atypical) may help in maintenance phase.
4. **Alternatives for treatment-resistant cases** - CLONAZEPAM, VERAPAMIL.

Current consensus: most effective treatment for acute mania is combination of:
- typical antipsychotic + mood stabilizer
- atypical antipsychotic + mood stabilizer

FDA-approved bipolar treatment regimens (marked as “*”):

<table>
<thead>
<tr>
<th>Drug</th>
<th>Manic</th>
<th>Mixed</th>
<th>Maintenance</th>
<th>Depression</th>
</tr>
</thead>
<tbody>
<tr>
<td>LITHIUM</td>
<td>⚫</td>
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<td>+</td>
<td>effective</td>
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<tr>
<td>CARBAMAZEPINE†</td>
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<td>effective</td>
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<tr>
<td>LAMOTRIGINE</td>
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<td>LAMOTRIGINE†</td>
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</tbody>
</table>

- in acute mania, VALPROATE can be titrated up to effective level more quickly than LITHIUM (i.e. lithium does not work immediately but should nonetheless be started early in anticipation of maintenance use!);
- antipsychotics or benzodiazepines are often coadministered to control behavior and psychosis.
- **LITHIUM** is first-line agent for long-term prophylaxis:
  - continue (after acute episode) mood stabilizer for at least 6 mo, then taper and stop.
  - mood stabilizer is restarted for recurrent episodes and maintained if episodes are < 3 yr apart.
  - maintenance with LITHIUM is initiated after 2 classic manic episodes < 3 yr apart.

N.B: mood stabilizers must be stopped during pregnancy (at least 1st trimester); for severe relapse electroconvulsive therapy is safer!

**Treatment for DEPRESSIVE episode**

- mood stabilizers (LITHIUM, LAMOTRIGINE) + antidepressants are preferred (antidepressants alone may propel patient into manic episode!)

**PROGNOSIS**

Prognosis is worse than of major depression!

- >90% patients after first manic episode have additional episodes of mania or major depression.
  - often, cycling between depression and mania accelerates with age.
  - unlike schizophrenia, many patients are socially and occupationally functional when medication is maintained (i.e. free of symptoms between episodes).
  - significant morbidity and mortality rates (mortality averages 2-2.5 times expected rate for that age)
  - attempted (25-50%); / completed (11%) suicide are both common during depressive phase.
  - homicide is also danger*.
  - e.g. delusional manic patient believed everyone was against him; he searched for rifle in order to defend himself and to get them before they get him
  - patients are at risk for drug addiction.
  - comorbid medical problems can deteriorate (poor compliance, generally impaired judgment, reckless behavior).

**BIPOLAR II DISORDER**

- at least one MDE + one hypomanic episode + absence of any manic or mixed episodes.
  - disorders officially recognized for first time in DSM IV.
  - often, switch follows circadian factors (e.g. going to bed depressed and waking early in morning in hypomanic state).

**EPIDEMIOLOGY**

- lifetime risk = 0.5%.
- men < women.

**CYCLOTHYMIC DISORDER**

- dysthymia with intermittent hypomanic periods + no MDE, manic, or mixed episodes* during first 2 years.
If such episodes occur after 2 years, more than one diagnosis may be made (e.g. cyclothymia and bipolar I disorder).

### Epidemiology
- Lifetime risk ≈ 1%
- Men ≤ women.
- Age of onset - teens → early adulthood.

### Treatment
- Primarily of education.
- Some patients with functional impairment require mood stabilizer therapy (e.g. Divalproex).
- Antidepressants frequently precipitate manic symptoms!
- Patients with artistic inclinations should be encouraged to pursue careers in arts (because excesses and fragility of cyclothymia may be better tolerated there).

### Prognosis
- 50% patients ultimately develop bipolar II disorder.

### Seasonal Affective Disorder (SAD)
- Form of MDD with seasonal pattern of exacerbation and remission (arises during autumn → winter and resolves during spring → summer).
- SAD is common in climates with long or severe winters.
- SAD appears to be triggered by alterations in circadian rhythm and sunlight exposure.
- More likely to report atypical symptoms (hypersomnia, increased appetite).
- Treated with bright light therapy (BLT) + antidepressant medication.
  *10,000 lux for 30-90 minutes daily, usually within hour of arising in morning.

Bibliography for ch. “Psychiatry” → follow this link >>