BIPOLAR DISORDERS

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INTRODUCTION
TEMPERAMENTS

1. Hyperthymic temperament

- Habitually active, amiable, and prone to jest
- Sanguine humor
- Extroverted, humorous, articulate, overoptimistic and care free
- Leadership positions or performer , politician

- Overconfident
- Full of plans
- Broad interests
- Overinvolved and meddlesome
- Uninhibited and stimulus seeking

2.melancholic

- Lethargic, sullen and given to brooding and contemplation
- Persistent depressive disorder in DSM-5
- Philosophy, arts, poetry and politics
- Melancholic and anxious temperament

3. Cyclothymic temperament

- Cyclothymic disorder: cyclic alternation between extroversion and introversion
- Composing music, writing poetry, painting

4. Irritable temperament

- Irritable, hostile, given to rage
- Borderline personality disorder
- Choleric humor
- Military career or revolutionary action
- Irritable cyclothymia

5. Depressive temperament:

- Gloomy, incapable of fun, complaining
- Humorless
- Pessimistic
- Guilt-prone, low self-esteem, and preoccupied with inadequacy of failure
- Introverted, restricted social life

- Sluggish
- Few but constant interests
- Passive and sensitive
- Reliable, dependable and devoted
- Hard working, dependable, sensitive to the suffering and needs of others

- Phlegmatic humor
- Indolent, irresolute, timid
- Avoidant or schizoid personality disorder
- Suitable for jobs that require long periods of devotion to meticulous details
- Shoulder the burdens of existence w/o experiencing its pleasures

INTRODUCTION

- Bipolar disorder type I
- Bipolar type II disorder
- Cyclothymia
- Bipolar spectrum (includes classic bipolar disorder, bipolar II, recurrent depressions –soft bipolar as in hyperthymic temperament-)

- Depressive episodes ➡ 3 times more than manic episodes
- More likely to seek help during depression
- 2-thirds misdiagnosed initially (MDD: the most common misdiagnosis)
- Correct diagnosis ➡ 8-10 years after the onset of illness
- Underdiagnosis of bipolar disorder is one of the greatest threats to public health

THE CLINICAL PRESENTATIONS
MANIC EPISODES

- Talkativeness
- Hyperactivity
- Rapid and loud speech
- Pressure of speech (hallmark of mania)
- Elevated, expansive or irritable mood (hallmark of a manic episode)

THE CLINICAL PRESENTATIONS
MANIC EPISODES

- The Elevated mood is infectious and euphoric
- Low frustration tolerance that lead to anger and hostility
- Labile emotion
- Rapid thought
- Distractable

THE CLINICAL PRESENTATIONS
MANIC EPISODES

- Flight of ideas
- Impaired concentration
- Self-confidence
- Delusions in 75 percent of patients
- Orientation and memory are intact except in delirious mania

THE CLINICAL PRESENTATIONS
MANIC EPISODES

- Impaired judgement and disinhibition
- Impulsivity
- Preoccupation with religious, political, financial, sexual, or persecutory ideas

THE CLINICAL PRESENTATIONS
DEPRESSIVE EPISODES
QUALITATIVE DIFFERENCES WITH MDD

- Substance abuse
- Psychotic symptoms
- Hx of postpartum depression especially with Psychotic Features
- A family hx of bipolar disorder
- A hx of antidepressant-induced hypomania
- Psychotic depression before 25 y

THE CLINICAL PRESENTATIONS

DEPRESSIVE EPISODES

QUALITATIVE DIFFERENCES WITH MDD

- Rapid onset and offset of depressive episodes of short duration (less than 3 months)
- Recurrent depression (more than 5 episodes)
- Seasonality
- Atypical depression
- Hyperthymic and cyclothymic temperament

THE CLINICAL PRESENTATIONS

DEPRESSIVE EPISODES

QUALITATIVE DIFFERENCES WITH MDD

- Repeated (at least 3 times) loss of efficacy of antidepressants after initial response
- Depressive mixed state (with psychomotor excitement, irritable hostility, racing thoughts, sexual arousal)
- Agitated depression

THE CLINICAL PRESENTATIONS

DEPRESSIVE EPISODES

QUALITATIVE DIFFERENCES WITH MDD

- Periodic impulsivity such as gambling,
  sexual misconduct, wanderlust, suicidal crisis
- Refractory depression (failed antidepressants from 3 different classes)
- Depression with erratic personality disorders

THE CLINICAL PRESENTATIONS

DEPRESSIVE EPISODES

DIFFERENTIATING CHARACTERISTICS OF BIPOLAR AND UNIPOLAR DEPRESSIONS

	Bipolar	**Unipolar**
Hx of mania or hypomania	Yes	No
Temperament and personality	Cyclothymic and extroverted	Dysthymic and introverted
Sex ratio	equal	Women > Men
Age of onset	Teens, 20s, 30s	30s, 40s, 50s

THE CLINICAL PRESENTATIONS

DEPRESSIVE EPISODES

DIFFERENTIATING CHARACTERISTICS OF BIPOLAR AND UNIPOLAR DEPRESSIONS

	Bipolar	Unipolar
Postpartum episodes	More common	Less common
Onset of episodes	Often abrupt	More insidious
Number of episodes	Numerous	Fewer
Duration of episode	3-6 mo	3-12 mo

THE CLINICAL PRESENTATIONS

DEPRESSIVE EPISODES

DIFFERENTIATING CHARACTERISTICS OF BIPOLAR AND UNIPOLAR DEPRESSIONS

	Bipolar	**Unipolar**
Psychomotor activity	Retardation > Agitation	Agitation > Retardation
Sleep	Hypersomnia > Insomnia	Insomnia > Hypersomnia
Family hx of Bipolar disorders	Yes (generally greater familial loading for mood disorders)	Only slightly
Family hx of Unipolar disorder	Yes	Yes

BIPOLAR DISORDER IN CHILDREN AND ADOLESCENTS

- Misdiagnose as a conduct disorder, antisocial personality disorder, Schizophrenia
- Symptoms may include: psychosis, substance abuse, suicide attempts, academic problems, philosophical brooding, OCD symptoms, multiple somatic complaints, marked irritability resulting in fights, antisocial behaviors

BIPOLAR DISORDER IN CHILDREN AND ADOLESCENTS

- Intriguing links between pediatric bipolar disorder and ADHD
- MDD is an unstable diagnosis in these ages.
- Depression + irritability, labile moods, explosive anger, questionable response to antidepressants or hypomanic switches, high recurrence rate, positive F.Hx

DIAGNOSIS
BID

- At least one manic episode

DURATION:

- Manic episode: 1 wk
- Hypomanic episode: 4 days
- Major depressive episode: 2 wk

DIAGNOSIS
BID

MANIC OR HYPOMANIC EPISODES SYMPTOMS:

Abnormally elevated or irritable mood (required)

Grandiose thoughts or increased self esteem

Decreased need for sleep

Pressured speech or hyper-talkativity

Racing and expansive thoughts or FOI

Distractibility

Hyperactivity (Increased goal-directed activity _socially, at work, school, sexually) or psychomotor agitation

Impulsivity / high risk activities

DIAGNOSIS
BID

Depressive episodes:

similar to MDE

with admixtures (FOI, increased drives and impulsivity in sexual and other domains)

Required number of symptoms:

at least 1 manic episode

abnormally elevated or irritable mood (required)

3 or more of the other symptoms (4 if irritable mood)

DIAGNOSIS
BID

Psychosocial impact

- manic episode: impaired functioning or needing hospitalization
- hypomanic episode: no impairment or need for hospitalization
- depressive episode: marked distress and/or psychosocial impairment

- *hyperthymic, cyclothymic and not uncommonly depressive temperament*

DIAGNOSIS
BIID

- Hypomania rather than mania
- Hypomania:
  associated with change in functioning
  observable by others
  not severe enough to cause marked impairment or to necessitate hospitalization.
- *Hyperthymic and cyclothymic temperament*

DIAGNOSIS
BMD WITH MIXED FEATURES

- Either depressive or manic/hypomanic episode
- Additional symptoms (2-4) of depressive or manic/hypomanic period
- Mania superimposed on a depressive temperament or using substance during mania

DIAGNOSIS
BID WITH RAPID CYCLING

- 4 or more mood episodes in 1 year
- 2 months or more period of partial/full remission between episodes
- Predisposing factors: female gender, hypothyroidism, menopause, TLE, substance abuse, Antidepressants
- *More prevalent in BIID

DIAGNOSIS
BID WITH MELANCHOLIC FEATURES

- Loss of pleasure or reactivity to pleasure
- 3 or more of the following:
  severe depression/ mood worse in AM/
  early morning awakening/ psychomotor disturbance/
  anorexia or weight loss/guilt.

DIAGNOSIS
BID WITH ATYPICAL FEATURES

- Mood reactivity
- 2 or more of following :

  increased appetite or weight/

  hypersomnia/

  leaden paralysis/

  rejection sensitvity

DIAGNOSIS
BID WITH ANXIOUS DISTRESS

- 2 or more following symptoms:

  Feeling tense

  Restlessness

  Difficulty with concentration due to worrying

  Increased fear w/o cause

  Fear of loss of control

DIAGNOSIS
BMD

- With mood congruent psychotic features
- With mood incongruent psychotic features
- With catatonia
- With prepartum onset: episodes occurs during pregnancy or within 4 wk after delivery

DIAGNOSTIC SPECIFIERS

With seasonal pattern

- Higher prevalence of manic episodes in the spring and summer
- Mostly for depressive episodes
- Pattern present for 2 ys or more

CYCLOTHYMIC DISORDER

- 2 Years or more (one or more for children) with depressive and hypomanic symptoms present 50% or more of the time
- Functioning impairment
- Specifier: with anxious distress

CYCLOTHYMIC DISORDER

- Trait bipolar condition
- Typically begins before 21 y/o
- Geogrophical instability
- Many often labeled borderline

D.DX

- Psychotic disorders

Overfamiliarity with strangers vs w/d

- Personality disorders

especially misdiagnosed as borderline personality disorder in those with cyclothymic, hyperthymic and dysthymic temperaments

Misdiagnosis with narcissistic and sociopathic personality disorders

DRUGS ,SUBSTANCES AND SOMATIC ILLNESSES THAT CAN INDUCE MANIA

- Steroid
- Amphetamine
- Cocaine
- Alcohol
- L-dopa
- Thyrotoxicosis
- SLE

- MS
- Tumors
- CPS
- AIDS
- Negative F.Hx
- Lower risk of recurrence
- Late life mania

COMORBIDITY

- 75%
- Men: substance use disorders (more than MDD)
- Women: anxiety and eating disorders (more than MDD)
- Panic disorders
- OCD (especially sexual and religious obsessions that wax and wane)
- Social phobia

ONSET

- 5-10 % of patients with an initial diagnosis of MDD have a manic episode 6-10 years later (mean age:32 years) / often after 2-4 dep episodes
- BID most often starts with depression (75% in women and 67% in men)
- Can be early as age 8 y/o
- Mania in older persons: medical conditions/ dementia

COURSE

- With progression, the time between episodes will decrease
- After 5 episodes interepisode interval stabilizes at 6-9 months

PROGNOSIS

- Poorer that MDD
- 40-50 % 2nd manic episode within 2 years
- Treatment improves prognosis
- 7 % no recurrence
- 45 % more than one episode
- 40% chronic disorder
- One third have chronic symptoms and evidence of significant social decline

- Comorbid SUD and anxiety disorders worsen the prognosis and increase the risk of suicide
- BIID: highest risk of suicide
- Chronic mania: 5% of BID
  recurrent manic episode on a a hyperthymic baseline/
  noncompliance/grandiose delusions

PROGNOSTIC INDICATORS

Factors of poor prognosis:

- Premorbid poor occupational status
- alcohol dependence
- psychotic feature
- depressive features
- Inter-episode depressive features
- male gendeR
- The earlier age of onset

Predictors of better outcome:

- A short duration of manic episode
- advanced age of onset
- few suicidal thoughts
- few coexisting psychiatric or medical problems

BIPOLAR DISORDER AND SUICIDE

- 20% of those who attempt suicide, eventually die because of suicide
- 50 % suicide victims die by their 1st suicidal act
- 50 % of suicide victims made at least one prior attempt

BIPOLAR DEORDER AND SUICIDE
RISK FACTORS

- MDE
- Manic episode with mixed features
- earlier age of onset
- higher frequency of episodes
- higher rate of rapid cycling course

- substance use and anxiety disorder comorbidity
- Insomnia
- Hopelessness
- agitation
- weight or appetite loss

- guilt feeling
- SI
- Depression with psychotic features
- Boredrline personality disorder
- cyclothymic temperament

- Previous suicidal attempt
- male gender
- positive f.hx in 1st and 2nd degree
- Abuse in childhood (physical or sexual)
- Severe negative life event

- Separation, widowhood, retirement, bereavement
- Feeling stigmatized
- Few days after hospitalization and unplanned discharge
- Older persons
- Minority groups (homosexuals and transgender)

- Healthcare professionals
- comorbid medical disorder
- Noncompliance
- Aggressive, impulsive-pessimistic traits, cyclothymic, irritable, depressive, anxious temperament

- Is path warm (**I**deation, **S**ubstance abuse,
  Purposeless –no reason for leaving or anhedonia,
  Anxiety-Agitation and insomnia, **T**rapped,
  Hopelessness, **W/D** , **A**nger,
  Recklessness, **M**ood changes)

- Losses, scandals or imprisonment rarely precipitate suicide in the absence of a psychiatric disorder
- Antidepressants and suicide
- More than one-third of DSM diagnosed unipolar MDD are in fact bipolar depression
- Treatment ➡ 70-80% risk reduction in suicidal behavior

BIPOLAR DEORDER AND SUICIDE

PEOTECTIVE FACTORS FOR SUICIDE

- Social support
- Pregnancy and postpartum period
- Large number of children
- Religious beliefs
- Physical activity
- Restricting lethal methods
- Optimistic traits
- Hyperthymic temperament
- Acute and long term tx

BIPOLAR DEORDER AND SUICIDE

PHYSICIAN FACTORS RELATED TO POOR RECOGNITION OF DEPRESSION AND PREVENTING SUICIDE:

- Lack of experience
- Insufficient knowledge about symptoms, tx and good prognosis in treated mood disorders
- Prejudice about mental illness
- Insufficient interview skills
- Lack of cooperation with psychiatrists
- Low level of empathy

TREATMENT

- Hospitalization for severe manic or suicidal patients
- Medications are tx of choice
- Needing indefinite maintenance pharmacotherapy
- 50% : seek treatment
- Less than One-third of recognized bipolar patients receive appropriate tx

- >50% of suicide victims contact health care 4 weeks before comiting suicide (rate of adequate pharmacotherapy is low)
- 60% nonadherent or poorly adherent
- Psychoeducation improves adherence

TERATMENT
ACUTE MANIA

- 1st line: lithium, divalproex, divalproex ER, olanzapine, risperidone, quetiapine, quetiapine XR, aripiprazole, lithium or divalproex with risperidone, lithium or divalproex with quetiapine, lithium or divalproex with olanzapine, lithium or divalproex with aripiprazole
- 2nd line: carbamazepine, carbamazepine ER, ECT, haloperidol, Lithium + divalproex
- Third line: chlorpromazine, clozapine, lithium or divalproex+haloperidol, lithium +carbamazepine

TREATMENT
ACUTE DEPRESSION

- Ist line: lithium, quetiapine, lamotrigine + lithium, lamotrigine, quetiapine, quetiapine XR, lithium or divalproex + SSRI, lithium or divalproex + bupropion, olanzapine +SSRI lamotrigine
- 2nd line: divalproex, carbamazepine, olanzapine, ECT, adjunctive SSRI to SGA, adjunctive modafinil, adjunctive pramipexole
- 3d line: lithium+carbamazepine, adjunctive NAC, adjunctive RTMS

- ECT: 1st line in 1st trimester of pregnancy or delirious mania

TREATMENT MAINTENANCE

- 1st line: lithium, lamotrigine, divalproex, olanzapine, quetiapine, risperidone LAI, aripiprazole, lithium or divalproex + quetiapine/ risperidone LAI, aripiprazole
- 2nd line: carbamazepine, lithium + divalproex, lithium +carbamazepine. Lithium or divalproex + olanzapine, lithium + risperidone, lithium + lamotrigine
- 3d line: risperidone, clozapine, ECT, omega 3, gabapentin

TREATMENT OF COMORBIDITIES

GAD:

- Pregabalin, quetiapine, gabapentin, Escitalopram, paroxetine, sertraline, agomelatine

Social anxiety disorder:

- CBT, pregabalin, gabapentin, SSRIs in non-responders

Panic disorder:

- valproate, gabapentin, quetiapine, risperidone, SSRI, clonazepam, alprazolam, lorazepam

PTSD:

- anticonvulsants, SSRIs + SGA, SGA

OCD:

- adjunctive treatment with lamotrigine, topiramate, risperidone, aripiprazole, olanzapine, quetiapine

MANAGEMENT OF AGITATION IN AN EMERGENCY SETTING

- Haloperiol + lorazepam
- Haloperidol + biperiden
- Haloperidol + promethazine
- Chlorpromazine

TREATMENT LIMITATIONS

- Lamotrigine and severe rash
- antidepressants and rapid cycling, mania and haypomania, mixed episodes (especially TCAs, MAOIs,SNRIs)
- Lithium and toxicity: vomiting and diarrhea, coarse tremor, agitation, dysarthria, drowsiness, lethargy, ataxia, polyuria, polydipsia, syncope, dizziness, arrhythmias.
- Valproate and weight gain, hair loss, PCOS
- CBZ and leukopenia

EPIDEMIOLOGY

- 50% of all depressions
- Majority of patients with postpartum depression
- Early negative life events (e.g. parental loss before adolescence) is a predisposing factor for mood disorders
- Sex: BID equal among men and women
- Manic episodes more in men

EPIDEMIOLOGY

- Depressive episodes more in women
- Manic episode with mixed picture(dysphoric mania and mixed depressive episode): more in women
- Rapid cycling: more in women
- Winter depression more in women
- Bipolar depression with atypical features more in women

EPIDEMIOLOGY

- Onset earlier than MDD (20 y/o)
- Onset in men 5 y earlier than women
- >50% : before 20 y/o
- Age of onset Recurrent unipolar MDE: 30-35 y/o
- Age of onset of single-episode major depression w/o F.Hx of mood disorders: some years later

- More common in divorced and single persons
- Higher than average incidence of BID in upper socioeconomic groups
- More common in under-graduated people
- BIID: above the average educational level, higher social classes, overrepresented among socially active, creative people

- Peak time for mania: summer
- Seasonal depression (fall-winter depression and spring-summer energetic period)
- Negative life events: cause or effect of the disorder?

GENETICS

- 7fold higher risk in 1st degree relatives
- Individuals with a few risk alleles have a spectrum trait, such as cyclothymic temperament
- Bipolar III disorder: Gene carrier depressed patients that predispose them to bipolar disorder (family history of bipolar disorder or a hx of hypomania or mania only in response to antidepressants)

- Patients with depression and a hyperthymic temperament are more likely to have a f.hx of BMD and to develop mania
- Migraine headache higher frequency in the families of bipolar probands(in particular biid)
- Cyclothymic, dysthymic and anxious temperaments elevated

GENETICS

- 70-80% etiology
- If one parent has a mood disorder , risk for child is 10-25%
- If both parents are affected : risk doubles
- More members affected: greater risk to the child especially if the affected is 1st degree relative
- Emphasize the risk rather than certainty of illness

- Use of such information in family planning is a highly personal decision
- Educate parents about age of onset, presenting symptoms and the importance of early recognition snd tx (emphasize on not being overly protective)

FAMOUS PATIENTS

- Tchaikovsky
- Lord Byron
- Ernest Hemingway
- Van Gogh

THANK YOU FOR YOUR ATTENTION.