Phenomenology

WHAT IS A MOOD?

Definition: the sustained feeling tone that prevails over time for a patient (anxious, panicky, terrified, sad, depressed, angry, enraged, euphoric, and guilty). At times the patient will verbalize this mood. Otherwise, evaluator must inquire or infer. Particular attention should also be given to the quality of mood, noting its depth, length of time it prevails, and the degree of fluctuation.

When we speak of a "mood disorder", we usually are referring to a sustained abnormality in the level of a person's mood. Most often we think in terms of too high, or too low a level, hence mania or depression.

Community Studies

Epidemiologic Catchment Area (ECA) Study
5% lifetime prevalence of depression
2:1 female to male ration
1% lifetime prevalence for bipolar disorder
socioeconomic factors not clear

National Comorbidity Study
7% lifetime prevalence
12% male, 21% female
only surveyed people under 55

		Depression	Mania
General		signs of poor self care, soft, slow speech, psychomotor retardation	flamboyant appearance, rapid, pressured speech, agitation or increased movement.
Emotiona	Mood	Dysphoric, angry or apathetic	Euphoric, irritable
	Affect	Blunted, sad, constricted	heightened, dramatic, labile
Thought	Process	Slowed process, thought blocking	flight of ideas, loose associations
	Content	Guilty, self-deprecating, suicidal ideation	grandiosity, delusions
Cognition		poor attention, concentration, registration, poor effort.	Distractible, poor concentration

Epidemiology

Etiology/Pathology

There is no single clear pathologic finding that correlates with clinical findings, but there are many associated findings, both macro- and microscopic, that give hints to the etiology of depression.

Gross Pathology & Physiology

Alterations in *circadian rhythms*, with *early morning awakening*, early fatigue during the day, and more REM sleep early on.

Strokes in certain areas of the brain (*dominant frontal or basal ganglia lesions*) have been shown to predispose to depression

Depressed patients do *not* show normal feedback of *HPA axis* with the *dexamethasone suppression test*.

Functional imaging in depressed patients shows *hypometabolism* in certain areas, especially in the prefrontal areas (orbital cortex, basal ganglia).

Microscopic

Most research is currently on the role of *neurotransmitters* in depression. Depression has been induced by depleting neurotransmitters (e.g. reserpine), and current medications that target neurotransmitters have been largely successful.

Metabolites of neurotransmitters have also been studied, such as MHPG (a metabolite of norepeniphrine). Findings have been inconsistent, but some findings indicate a correlation with depression. Some studies have shown decreased MHPG levels in depressed patients, increase in MHPG in bipolar patients switching to the manic phase, and some evidence that pre-treatment levels of MHPG may predict response to medication.

However, a good deal of evidence suggests that the story goes way beyond neurotransmitters (see below).

Genetics

Family studies have shown that mood disorders cluster in families, with increased rates in first degree relatives.

Twin studies have shown a higher rate of mood disorders in monozygotic than dizygotic twins, which indicates a strong genetic component in mood disorders.

Linkage studies have been inconsistent with no clear location implicated in the genetics of mood disorders.

Neurochemical Hypotheses

Catecholamine Hypothesis (NE, 5-HT, DA, Epi)

↓ catecholamines = depression

↑ catecholamines = mania

Receptor Hypothesis

Suggestion that defect in mood disorders is in the regulation of receptors, not neurotransmitters.

Supported by evidence that shows that medications for depression and mania induce changes in pre- and post-synaptic density of receptors.

Post-receptor Hypothesis

G-proteins are linked to most monoamine receptors.

Changes in second messenger systems have been implicated in mood disorders and their recovery with pharmacological treatment.

Diagnoses and Criteria (DSM-IV)

Episodes versus disorders: Episodes are listed first for convenience. They do not exist as separate disorders, but rather define essential clusters of symptoms that will be used in defining the actual disorders.

THE EPISODES

Major depressive episode

-time: at least 2-weeks

-represents a change from previous functioning

-Symptom list (5 or more, 1 has to be depressed mood or anhedonia)

-mnemonic: "SIG E CAPS":

- Sleep
- Interest
- Guilt
- Energy
- Concentration
- Appetite

Manic Episode

-Time: 1 Week any duration if hospitalization is necessary)

-Symptom list (3 or more--four if the mood is only irritable):

- grandiosity
- need for sleep
- pressured speech
- flight of ideas
- distractibility
- ↑activity/agitation
- risky activities

Mixed Episode

Symptoms of both Major Depressive Episode

Hypomanic Episode

Basically the same as Manic Episode, except:

-can last only 4 days

THE DISORDERS

Depressive Disorders

Major Depressive Disorder

Conceptually: this is the "classical" depressive diagnosis.

Major Depressive Episode (above).

Rule out:

Specifiers for Major Depression

Level of Severity
Course Specifiers
Special types:

* Dysthymic disorder

* Depressive Disorder Not Otherwise Specified
The Wastebasket Category for disorders

Bipolar Disorders

Bipolar I Disorder

Classic Manic Depressive Disorder
Has to have had at least one Manic or

Bipolar II Disorder

One or more Major Depressive Episodes, and

Cyclothymic Disorder

Essentially "little bipolar", with mood fluctuations,
Episodes of hypomanic

Bipolar Disorder Not Otherwise Specified.

The Wastebasket Category for disorders with depressive features that do not meet the criteria

OTHER MOOD DISORDERS

Mood Disorder Due to a General Medical Condition.

As the name implies. The important thing is that the mood disorder is judged to be directly related to the medical condition (not just a "reaction" to a disorder, etc.)

Symptoms can be manic, depressed or mixed
-don't have to meet full criteria

Substance-Induced Mood Disorders

Mood symptoms occur directly due to a substance.
Commonly during substance intoxication or withdrawal.
only diagnose when the mood symptoms are:
1) in excess of what you'd expect for that substance
2) The symptoms are bad enough to warrant independent attention.
Can also be from normal use of a substance.
Not only while delirious.

Mood Disorder Not Otherwise Specified.

Wastebasket for when you can't choose between Depressive Disorder or Bipolar as the main problem.

Important Differential Diagnoses

PSYCHIATRIC DIAGNOSES

(1) Adjustment Disorders

To cover concept of a response to an psychosocial/environmental stress.
Usually manifests as some emotional symptoms, but not the whole spectrum of a mood disorder.
If meets criteria for another psychiatric disorder (like major depression or bipolar disorder), then would diagnose that disorder instead of adjustment disorder.

(2) Bereavement (Grief)

Similar rationale to the Adjustment Disorders.

(3) Anxiety disorders

some overlapping symptoms (e.g. Racing thoughts, sleep disturbance. Anxiety itself can be a symptom of depression).
primary difference is the prominence of mood (dysphoria, anhedonia) as a major symptom

Is commonly comorbid, however, so both may occur (see below).

(4) Psychotic disorders

Schizoaffective: really a cross between schizophrenia and mood disorders, but *psychotic symptoms* occur in schizoaffective absent of any mood symptoms at the time.

partially a judgement call: can you say that the mood symptoms and the psychotic symptoms are pretty equal in importance

(5) Abuse disorders

Many substances can cause depressive symptoms either through use or during withdrawal.

The problem of comorbidity:

For example, are alcoholics "self-medicating" a depression, is the depression simply secondary to the alcohol, or are the two co-occurring (see below under Comorbid Disorders)?

(6) Personality disorders

Some, such as borderline personality, can frequently show depressive symptoms.

Difference is in time-major depressive episodes are stable over the course of days to weeks, whereas mood lability as a part of a personality disorder tends to vary rapidly throughout the day.

Frequent comorbidity as well.

MEDICAL/OTHER DISORDERS

Many medical illnesses can mimic mood disorders.

Concepts of secondary mood disorders, masked disorders versus mimicry.

"Secondary" implies direct causation of a "true" mood disorder by a physical phenomenon.

Ex. There is a sizeable literature regarding the comorbidity between cerebrovascular accidents and depression, particularly those occurring in the dominant fronto-parietal area.

"Masked" is a (probably incorrect) term implying that a disorder is presenting in an atypical way.

Ex. The phenomenon of a depressed patient (usually elderly) presenting with a variety of physical complaints, but really having a depression. In this case, there probably isn't s "real" physical disorder.

Often, medical disorders can have one or more depressive symptoms, but generally not enough to meet criteria for a major mood disorder.

Cancer

Patient with adenocarcinoma of the pancreas can have depression-type symptoms (fatigue,

poor appetite) as presenting symptoms of the disorder

This should be differentiated from cases of comorbidity between psychiatric and medical disorder

Neurological Conditions

Dementias:

Can present with social withdrawal, emotional distress, that may be misperceived as a mood problem.

Parkinson's Disease:

The bradykinesia that occurs can be interpreted as the psychomotor retardation of depression.

Multiple Sclerosis:

Can often get a phenomenon of emotional lability as part of a pseudobulbar palsy. This can be misinterpreted as depression, but tends to be transient and to lack much emotional content.

Once again, many of these disorders can commonly co-occur with depression

Endocrine Conditions

Most commonly cited is *hypothyroidism*, which can cause a depression-like condition that is unlikely to resolve unless the primary disorder is corrected.

A variety of adrenal problems, such as Cushing's, have been associated with both depressive- and manic-like conditions.

Generalized Anxiety Disorder: Twin studies suggest a common genetic origin with depression. Differentiation of the two disorders may be decided by environmental factors.

Mixed Anxiety-Depression: Observations of the common overlap between anxiety and depressive symptoms lead to the addition of this category to the DSM-IV. The presence of this common syndrome may predict a poorer course of illness

(2) Substance-induced disorders

In addition to the substance use disorders mentioned above, a wide variety of substances have been listed as having effects on mood.

Some had been implicated in causing "true" mood disorders (ex. Reserpine causing depression). More often cause some symptoms associated with depression. Probably not so important to argue whether these substances "cause" secondary mood disorders or cause mood disorder-like syndromes, as the treatment is the same: try to remove the offending substance.

In some cases this cannot be done (ex. A patient requiring high dose steroids). In that case, treatment with an antidepressant may help.

Self-medication: Perhaps alcoholics are "medicating" their mood disorder. There is little data to support this- mostly based on clinical observation.

Forme frustre: Perhaps alcoholism is part of a depressive spectrum of disorders. Evidence for this is mainly from family data, which shows co-transmission of both disorders.

Secondary mood disorders: Perhaps alcohol causes depression. The strongest

Comorbid Disorders

PSYCHIATRIC

(1) Anxiety

Anxiety is so frequently comorbid with depression that some question whether the two can really be considered distinct disorders at all. An example is *Panic disorder*. As many as 50% of panic disorders have comorbid depression. This may negatively

effect prognosis and response to treatment.

(2) Substance Abuse

The ECA study found that about 13% of those with substance abuse of dependence also have a life diagnosis of a mood disorder. Similar results have been found in other countries. Alcoholism predicts a worse outcome for a mood disorder. Alcoholics may be half as likely as other people to recover from an episode of major depression after even 10 years. Some theories regarding the relationship between mood disorders and alcoholism include **self-medication, *forme frustre*, and secondary mood disorders**. *Twin studies* suggest that the substantial comorbidity between major depression and alcoholism results primarily from genetic factors influencing the risk to both disorders. This does not mean, however, that major depression and alcoholism are manifestations of the same disorder. The two disorders appeared to have both common and separate genetic factors that independently influenced the liability to either disorder. Simultaneous support of different theories underscores the heterogeneity of the mood disorders.

Other Substance Use Disorders include Nicotine Dependence, Cocaine, and Opioids. There is a high prevalence of depression in smokers, and this may negatively influence attempts to quit.

(3) Psychotic Disorders

It is difficult to judge comorbidity, as one can have psychotic depression. Symptoms of psychotic depression tend to overlap with Schizoaffective Disorder. The presence of psychotic features, whether as a symptoms of the mood disorder, or independently of it, has an adverse affect on the mood disorder.

Other Psychiatric Disorders where depression is common:

Somatoform Disorders: Particularly hypochondria and somatization disorder.

Eating Disorders: Particularly anorexia nervosa.

Attention Deficit Disorders: Perhaps a third of children

(4) Personality Disorders

There are high rates of comorbidity between personality disorders and major depression, with a range from 30% to almost 90%. Inpatient samples typically see comorbidity most often reported in the dramatic types of personality disorders (cluster B: histrionic, narcissistic, borderline, and antisocial personality disorders) type, as the impulsive behaviors associated with these personality disorders are likely to lead to hospitalization. Outpatient samples are more likely to show "cluster C" or "anxious-fearful" types. What is the relationship between the two disorders? It may be an artifact: Individuals suffering from major depressive episode may overestimate their own personality pathology.

Or, the definition of the two disorders may so overlap as to make discrimination between the Axis I and Axis II disorder nearly impossible.

If the comorbidity of the two disorders is a real phenomenon, one can imagine causality occurring in either direction. Individuals with personality disorders may be at a higher risk for depression; however, individuals with depression, particularly chronic or recurrent types, may be more likely to develop personality disorders. Alternatively, depression and personality disorders can be imagined as different manifestations of more basic characteristics. For example, the relationship may be between depression and tendencies towards anger attacks.

It is generally believed that depressed patients with a comorbid personality disorder are less likely to respond to somatic treatments. Few controlled studies have tested this belief; naturalistic studies, however, tend to support this assumption. This poorer response to treatment may, in part, reflect a greater severity of illness that results from the combination of major depression and a personality disorder. Some studies also suggest that depressed patients with borderline personality features may preferentially respond to monoamine oxidase inhibitors. A number of investigators have reported a relationship between comorbid borderline personality disorder, depression, and increased risk of suicide.

Medical Outcomes Study (Wells et al.,1989)

Studied more than 22,000 patients receiving care from 523 clinicians.

Focused on five specific diseases: **myocardial infarction, congestive heart failure, hypertension, diabetes and depression.**

Additive effect on patient's functioning when depression and other chronic medical illnesses were combined, suggesting a worse course for the medically comorbid depressed patients.

In a 2-year follow-up, they found that certain medical disorders predicted a worse course of depression, whereas others did not. The most adverse association was between myocardial infarction and depression:

DEPRESSION IN THE MEDICALLY ILL

Depression common in medical patients. Two to four percent of medical patients in the community, 5-10 percent of primary care patients, and 10-14 percent of medical inpatients are depressed. It is often unrecognized and untreated in the medical population. Such inadequate treatment may in part reflect the obsolete view that depressive symptoms with a clear cause are not the same as "clinical depression." Comorbid medical illnesses predispose an individual to a worse course of major depression.

Cardiovascular disease
- Cardiomopathy
- Cerebral ischemia
- Congestive heart failure
- Myocardial infarction

Neurological Disorders
- Alzheimer's disease
- Multiple sclerosis
- Parkinson's disease
- Head trauma
- Narcolepsy
- Brain tumors
- Wilson's disease

Cancer
- Pancreatic cancer
- Lung cancer

Endocrine disorders
- Hypothyroidism
- Hyperthyroidism
- Cushing's disease
- Addison's disease

Hyperparathyroidism

Hypoparathyroidism
- Hypoglycemia

Pheochromocytoma
- Carcinoid
- Ovarian failure
- Testicular failure

Infectious diseases
- Syphilis
- Mononucleosis
- Hepatitis
- AIDS
- Tuberclulosis
- Influenza
- Encephalitis
- Lyme disease

Nutritional deficiencies
- Folate
- Vitamin B12
- Pyridoxine (B6)
- Riboflavin (B2)
- Thiamine (B1)
- Iron

Drugs of Abuse
- Phencyclidine
- Marijuana
- Amphetamines
- Cocaine
- Opioids
- Sedative-hypnotics
- Alcohol

Antihypertensive drugs

Some medical disorders and medications associated with depression.

Course and Prognosis of the Mood Disorders

MAJOR DEPRESSION

(1) Recovery from an episode

Depression has usually been characterized as a self-limited disease, with an average duration of six to nine months. Newer studies, however, which employ prospective designs, suggest that a significant number of patients recover more slowly, or do not ever recover fully. In the Collaborative Depression Study (CDS), the greatest probability of recovery was early in the course of the illness, while chances of recovery less dramatic if the patient hadn't yet recovered in the 1st year.

Predictors of poor recovery included:

Long duration of illness;
Married status;
Inpatient hospital status at the time of intake;
Low family income; and
The presence of other psychiatric disorders.

Collaborative Depression Study (CDS):

Multi Center Naturalistic Study of the Course of Depression.

54% of the patients recovered within the first six months of the study.

Approximately 70% recovered within one year.

81% were recovered after two years, 87% after 4 years and 88% after five.

Thus, only 18% of the patients still depressed after one year recovered by year five.

(2) Risk of relapse

20% to 30% for patients who recover from a depressive episode risk relapse. Predictors of relapse include clinical factors and demographic factors. Clinical factors include alonger length of the index episode and history of multiple episodes. Demographic factors include older age and lower family income.

(3) Recurrence

A number of studies suggest that depression, for many, may be a lifetime illness. Significant numbers of patients experience multiple episodes of depression. The greatest risk of recurrence seems to be after three or more episodes. Others never fully recover from their illness, but may stabilize at a level of dysthymia or sub-syndromal depression.

(4) Course Modifiers

Double Depression is the concurrent presence of both dysthymia and major depressive disorder. By definition, dysthymia and major depression can only be recognized as coexistent if the dysthymia precedes the episode of major depression, or if there has been remission from major depression for at least two months. In double depression, the episodes of major depression appear to be superimposed upon a more chronic

Studies suggest that a person with double depression recovers more easily from a major depressive episode than a person with major depression alone. However, recovery is not to a

depression.

BIPOLAR DISORDER

(1) Recovery

from an episode of mania is usually thought to be around 4 months, with great variance. Predictors of good recovery include:

Symptoms. Patients with "pure" mania seem to recover faster and more completely than patients with mixed or cycling symptoms; and

History of previous mood episodes (both depressive and manic episodes).

(2) Relapse

In one long term study (@ 20 years), 85% of bipolar patients relapsed. The number of symptom free intervals tends to decrease over time. The predictors of relapse are not clear.

Some proposed predictors include:

low vocational advancement at illness onset
depression
number of previous episodes
mixed symptoms
comorbidity (esp with alcoholism)
psychotic features when manic
interepisode features.

Treatment

DEPRESSION

SIDE EFFECTS AND RISKS OF ANTIDEPRESSANTS:

Predictable: Due to a receptor interaction, eg., , Anticholinergic effects, adrenergic effects and serotonergic effects.

(1) Pharmacological Treatment:

Antidepressant classes include tricyclics, monoamine oxidase inhibitors, serotonin reuptake inhibitors and others. Mechanism of action of these drugs includes catecholamine effects, serotonin effects, and some newer theories of action. Overall, there is a 70-80% response rate to these drugs when used to treat major depression. They are also used for treatment of anxiety disorders and other disorders. When considering pharmacological treatment, it is important to consider the following clinical principles: targeting symptoms, response time of medications, the option of psychotherapy. Side effects and risks must also be considered, including the **predictable effects, drug interactions, idiosyncratic effects,**

and allergic reactions.

(2) Psychotherapy

Cognitive-Behavioral Therapy (CBT) is based on learning theory. This states that we learn to think a certain way and develop automatic thoughts and responses to situations. Depressive ways of thinking become habitual. What we learn can be unlearned through practice. CBT is an active therapy with lots of homework and assignments.

Interpersonal Therapy (IPT) is based on notion of depression as response to loss or perceived loss in social network. It is also very active and practice based.

Other psychotherapies shown to be effective include **Psychodynamic Therapy and Marital/Family Therapy.**

When to choose meds versus psychotherapy?

The weight of data supports the following conclusions:

Medication is superior to therapy for severe depression.

Medication and therapy is probably equal for mild to moderate depression.

Combination of medication and therapy may confer an

Commonly used drugs for treating depression				
	Class	$t_{½}$	Metabolism	Side Effects
Fluoxetine (Prozac, others)	Selective Serotonin Reuptake inhibitors (SSRI)	2-3 days (+ active metabolite, 7-10 days)	95% protein bound, liver met.: P-450 2D6 inhibition	nausea, vomiting, diarrhea, anorexia
Paroxetine (Paxil)		@ 1 day	95% protein bound, less affinity for p-450 inhibition.	
Sertraline (Zoloft)				
Citalopram (Celexa)				
Fluvoxamine (Luvox)		15 hours	80% protein bound, little P-450 2D6 inhibition, but does inhibit 1A2, 2C9, 3A4.	
Venlafaxine (Effexor)	Serotonin (5HT) and Norepinephrine (NE) Reuptake inhibitor	5 hours	25% protein bound, inhibits P450 2 D6.	SSRI side effects, + increased BP.
Mirtazapine (Remeron)	?Antagonism of presynaptic receptors: increases 5HT and NE	20-40 hr	85% protein bound. Extensively metabolized in the liver; excreted in both the urine (75%) and feces (15%).	Sedation, weight gain, postural hypotension.
Nefazodone (Serzone)	SSRI + $5HT_2$ postsynaptic blockade	2-4 hours	99% protein bound, inhibits P-450 3A4	Nausea, vomiting, sedation.
Trazodone		6 hours	90% protein bound.	Sedation, postural hypotension
Buproprion (Wellbutrim)	dopamine agonism, ? Norepinephrine effect?	6-24 hours	80% protein bound	anxiety, agitation, insomnia.
Amitriptyline, Doxepin, imipramine, desipramine	Tricyclic antidepressants: inhibit reuptake of norepinephirne,	15-20 hours	liver metabolised, high individual variation	sedation, anticholinergic effects, weight gain, orthostatic hypotension.
nortriptyline, maprotiline		1-2 days		
protriptyline		3 days		
phenelzine, tranycypromine	monoamine oxida oxidase inhibition	3 hours	liver metabolism, lots of drug interactions	orthostatis, dizziness, anticholinergic effects. Tyramine-cheese reaction.

BIPOLAR DISORDER

Treatment for bipolar disorder is much more pharmacologically based than major depression.

First line treatment for acute mania is **lithium**. The mechanism of action is poorly understand-probably at the level of a second messenger system (intracellular adenylate cyclase and phosphoinositol intracellular). Because there is a narrow range between the therapeutic and toxic doses of lithium, blood level monitoring is key. Additionally, there is wide variability of lithium pharmacokinetics among different individuals; thus optimum doses for an individual patient cannot be based on the dosage administered. While there is a 60% response rate overall, Lithium's efficacy is slow-- it works in about 7-14 days. Lithium has many side effects and risks, which are summarized in the table below. Diuretics and NSAIDS such as indomethacin may increase lithium levels in the blood. Used with antipsychotics may increase risk for neuroleptic malignant syndrome (see under Antipsychotics in Psychosis Section).

A note on Lithium: Although lower plasma levels are associated with less side effects, there is strong evidence that levels in the range of 0.8 to 1.0 mEq/L are more effective, both for acute manic and for preventing relapse. Treatment with lithium should not be

Antipsychotics, formerly haloperidol, now more likely atypical antipsychotics such as **olanzapine**, are also used to treat acute mania. Haloperidol works very rapidly (within hours or less). The mechanism is probably through sedative effect, not antipsychotic (since antipsychotic effect should take weeks). Haloperidol is not used for maintenance, but the atypicals are, and Olanzapine is now generally considered a "first line" treatment for bipolar disorder.

Thirdly, **sedatives** such as Lorazepam (Ativan) and Clonazepam (Klonopin) may be as rapid, as effective had safer than antipsychotics. Klonopin is sometimes used also for maintenance, but is probably not as effective as other choices. Usually, high doses are recommended.

For maintenance/prevention of relapse, **lithium** (see above) is the first choice. Other treatment includes **anticonvulsants**, such as **carbamazapine** and **sodium valproate**, and **atypical antipsychotics**, such as **olanzapine**.

Overall, efficacy of **carbamazapine** is 25-50%; it may be especially effective for dysphoric-type or mixed symptom mania. A summary of side effects is provided in the chart below. The most common side effect is sedation; the most serious side effect is agranulocytosis. Patients should be warned of symptoms of bone marrow suppression (e.g.,

The mechanism of action of carbamazapine may relate to the process of "kindling"— an idea derived from seizures in which repetitive subthreshold electrical stimulation of the brain eventually may lead to either a behavioral or a convulsive response. In

fever, sore throat, petechiae). Carbamazapine induces its own metabolism through induction of liver enzymes; thus, drug interaction is common. Some drugs are metabolized faster in the presence of carbamazapine, including oral contraceptives, corticosteroids, theophylline, warfarin, and haloperidol. Additionally, many drugs can raise carbamazepine levels, including cimetidine, danazol, d-propoxyphene, diltiazem, verapamil, isoniazid, and erythromycin.

Valproate's mechanism of action ispresumably similar to carbamazepine. Evidence of efficacy against mania has recently shown valproate to be similar to lithium in a large placebo controlled study. Valproate may be particularly effective for rapid cycling. A summary of side effects is provided in the chart below. The most common side effect is sedation; the most dangerous side effect is hepatotoxicity. Valproate can cause neural tube defects (spina bifida, anencephaly) in pregnancy.

Newer anticonvulsants, such as gabapentin and lamotrigine are promising for maintenance treatment of bipolar disorder, but more studies must be done.

Drugs commonly used to treat Bipolar Disorder

	half life	time to steady state	common side effects	serious side effects
Lithium	24 hours	4-6 days	nausea, tremor, increased urination and thirst.	CNS toxicity, renal toxicity
Valproic Acid (Depakene, Depakote)	5-13 hours	2-5 days	nausea, vomiting, drowsiness, tremor, dizziness.	Liver toxicity
Carbamazepine (Tegretol)	12-17 hours	3-5 weeks	drowsiness, dizziness, ataxia, nausea.	Thrombocytopenia
Olanzapine (Zyprexa)	21-54 hours	1-2 weeks	sedation, dry mouth.	Tardive dyskinesia, neuroleptic malignant syndrome