Bipolar Disorder

This article refers to the International Classification of Diseases 10th edition (ICD-10) which is the official classification system for mental health professionals working in NHS clinical practice. The literature occasionally refers to the Diagnostic and Statistical Manual of Mental Disorders (DSM) classification system which - whilst used in clinical practice in the USA - is primarily used for research purposes elsewhere. Bipolar disorder is a chronic episodic illness associated with behavioural disturbances. It used to be called manic depression. It is characterised by episodes of mania (or hypomania) and depression. Either one can occur first and one may be more dominant than the other but all cases of mania eventually develop depression.

Types of bipolar disorder

In the 1960s manic-depressive psychosis was divided into unipolar depression (patients with mainly depression), unipolar mania (patients with mainly mania) and bipolar disorder (patients with both depression and mania). This has now mainly been superseded by division into bipolar disorder types I and II.\[^1\]

- **Bipolar I**: this type presents with manic episodes (most commonly interspersed with major depressive episodes). The manic episodes are severe and result in impaired functioning and frequent hospital admissions.
- **Bipolar II**: patients do not meet the criteria for full mania and are described as hypomanic. Hypomania in comparison to mania has no psychotic symptoms and results in less associated dysfunction. This type is often interspersed with depressive episodes.

Further details of how the two subtypes relate to current diagnostic systems can be found in the Diagnosis section.

It is important to note that the diagnosis of bipolar disorder should not be made if symptoms are thought to result from drug ingestion or drug withdrawal.\[^2\]

Epidemiology

- There is limited information available but international studies suggest a lifelong prevalence rate of bipolar disorder of 2.4%.\[^3\]
- A UK study suggested that between 3.3% and 21.6% of primary care patients with unipolar depression may have an undiagnosed bipolar disorder.\[^4\]
- The lifetime rates of bipolar I are higher in males whereas the rate of bipolar II is higher in females.\[^3\]
- Relatives of people with bipolar disorder are five to ten times more likely to have bipolar disorder themselves.\[^5\]
- Anxiety and substance misuse are common associated conditions.

Presentation\[^5\]

**Manic phase**

Mania is characterised by elevated mood and increase in quantity and speed of physical and mental activity. Self-important views and ideas are greatly exaggerated. Some patients may be excessively happy, whilst others may be irritable and easily angered.
During the manic phase

The following may be present:

- Grandiose ideas.
- Pressure of speech.
- Excessive amounts of energy.
- Racing thoughts and flight of ideas.
- Overactivity.
- Needing little sleep, or an altered sleep pattern.
- Easily distracted - starting many activities and leaving them unfinished.
- Bright clothes or unkempt.
- Increased appetite.
- Sexual disinhibition.
- Recklessness with money.

In severe cases there may be grandiose delusions (e.g., belief that they are world leaders or monarchs), auditory hallucinations, delusions of persecution and lack of insight. The lack of insight is very dangerous as patients are unable to see the need for them to change their behaviour.

Hypomanic phase

Hypomania is a lesser degree of mania with persistent mild elevation of mood and increased activity and energy but without hallucinations or delusions. There is also no significant effect on functional ability.\[2\]

Depressive phase

In the depressive phase, patients experience low mood with reduced energy. Patients have no joy in daily activities and have negative thoughts. They lack facial expressions and have poor eye contact and may be tearful and unkempt. Low mood is worse in the mornings and is disproportionate to the circumstances. There may be feelings of despair, low self-esteem and guilt for which there may be no clear reason. There may be weight loss, reduced appetite, altered sleep pattern with early morning wakening and loss of libido.

In severe cases there may be delusions of persecution or illness or impending death. Patients may become unwell through self-neglect - e.g., not eating or drinking.

Psychosocial functioning

Bipolar disorder can have a detrimental effect on psychosocial functioning. It is important to ask specifically about relationship difficulties and work difficulties.\[6\]

Diagnosis\[1\]

ICD-10 requires at least two episodes in which a person's mood and activity levels are significantly disturbed (one of which must be mania or hypomania).\[8\] In comparison, the DSM-5 requires only one episode of mania without depression or one episode of hypomania with a single episode of major depression and divides bipolar disorder into types I and II. ICD-10 further divides bipolar disorder into:

- Currently hypomanic
- Currently manic
- Currently depressed
- Mixed disorder
- In remission

Three of the following symptoms confirm mania:

- Grandiosity/inflated self-esteem.
- Decreased need for sleep.
- Pressured speech.
- Flight of ideas (rapidly racing thoughts and frequent changing of their train of thought).
- Distractibility.
• Psychomotor agitation.
• Excessive involvement in pleasurable activities without thought for consequences (eg, spending spree resulting in excessive debts).

There may also be psychotic symptoms - eg, delusions and hallucinations. The manic episode is mixed if there are associated depressive symptoms.

Adults presenting in primary care with depression should be asked about previous periods of overactivity or disinhibited behaviour. If the overactivity or disinhibited behaviour lasted for four days or more, referral for specialist mental health assessment should be considered.

Clinical course

• Frequency and duration of episodes are variable.
• The symptoms of mania (or hypomania) and the presence of depressive symptoms may vary from day to day and also within the day.
• Between episodes patients may lead a normal work life and a normal lifestyle.
• 10-20% have rapid cycling - defined as four or more cycles of depression and mania a year, with no intervening asymptomatic episodes. [2, 9]

Differential diagnosis [4]

• Hyperthyroidism or hypothyroidism.
• Anorexia nervosa.
• Cerebrovascular event.
• Dementia.
• Other psychiatric disorders - eg, schizophrenia, schizoaffective disorder, cyclothymia.
• Medications - eg, steroids, isoniazid, L-dopa, sympathomimetic amines.
• Chronic kidney disease.
• Acute drug withdrawal or illicit drug ingestion.
• Cerebral insults - eg, neoplasm, infarcts.

Management [1]

The basis to any successful management plan is development of good rapport and a trusting relationship with the patient and their carers. Patients require educational information regarding the diagnosis and management strategies. Shared care protocols may be available and patients should have access to community mental health teams.

In primary care, the clinician’s role is to maintain an ongoing relationship with the person and their family/carers, help them to follow care plans devised in secondary care, institute crisis plans when appropriate to do so and monitor treatment.

For depressed patients, clinicians in primary care should consider referral to the Mental Health Team in the following circumstances:

• Severe depression.
• Patient deemed a danger to themself or others.
• Poor or partial response to treatment.
• Significant decline in function.
• Depression associated with a period of overactivity or disinhibited behaviour lasting more than four days.
• Poor adherence to treatment.
• Intolerance to medication.
• Comorbid misuse of alcohol or drugs.
• Planning to stop medication after a period of stability.
• Bipolar disorder in pregnancy or if a woman is planning pregnancy.

Most of the evidence for the treatment of bipolar disorder is mainly for bipolar I disorder and may not be easily extrapolated to bipolar II disorder.
Non-pharmacological methods

- Education regarding diagnosis, treatment and side-effects.
- Good communication.
- Self-help groups.
- Support groups.
- Self-monitoring of symptoms, side-effects and triggers.
- Coping strategies.
- Psychological therapy.
- Encouragement of engagement in calming activities.
- Telephone support.

Psychological therapies have been shown to be beneficial - eg, cognitive behavioural therapy which helps to identify triggers and how to avoid them. Other therapies which may help include cognitive interpersonal therapy and behavioural couples therapy.

Pharmacological management

Patients who present with an acute episode should be followed up once a week for six weeks and then every four weeks for the first three months.

Management of a first manic episode

- Manic episodes require urgent control and patients may be violent. Liaise with a consultant psychiatrist - always consider hospital admission (as insight is usually lost) and record assessment of any suicidal ideas.
- Aims of treatment are to reduce symptoms rapidly and ensure safety of the patient and others. If the patient is violent or poses a danger to self or others then refer urgently for psychiatric assessment and consider use of the Mental Health Act (MHA) if they are unwilling to be admitted voluntarily.
- Try to convince patients to have oral therapy voluntarily. In A&E, therapy can be given under coercion under Common Law if it is deemed that not doing so would cause harm to the patient or to others.[11]
- If acute control is needed then use one or more of the drugs discussed below. Use oral preparations in preference to intramuscular (IM), as absorption varies and it is therefore difficult to determine response. Rapid tranquilisation (parenteral administration of tranquillising drugs) may be needed - remember, if the patient refuses, you may need either to use Common Law (allows treatment in an emergency) or to use the MHA. Ensure circumstances are well documented, including whether the MHA or Common Law was used.
The following represents a summary of current guidance on the management of bipolar disorder:[1]

**Treatment of a subsequent acute manic episode**

- If patients are already on an antipsychotic and develop a further manic episode then either the dose of the antipsychotic should be increased to the maximum licensed dose or it should be increased to the maximum tolerated dose. Drugs commonly used are haloperidol, olanzapine, quetiapine and risperidone. If one antipsychotic is ineffective it is worth changing to a different one.
- If the second antipsychotic is ineffective at maximum licensed or tolerated dose, consider adding lithium. If lithium is inappropriate (eg, the patient refuses regular monitoring) consider adding valproate.
- Valproate should not be used routinely in females of child-bearing potential and if it is used then patients need to be counselled about alternative forms of contraception.
- If a patient with hypomania or mania is taking an antipsychotic with an antidepressant, the antidepressant should be stopped.
- If patients have a further manic episode on lithium, the levels should be checked and the dose increased if possible, or an antipsychotic can be added.
- If the patient is on valproate then the dose should be increased until symptoms abate or side-effects prevent further increases, in which case an antipsychotic should be added (eg, olanzapine, quetiapine or risperidone).

Rarely, rapid tranquilisation of patients with mania is required. This can be achieved with antipsychotics, benzodiazepines or antihistamines given orally, IM or, in exceptional circumstances, intravenously (IV).[12] However, these methods do not provide a long-term solution. See separate Rapid Tranquilisation article.

**Treatment of an acute depressive episode**

- Primary care clinicians should consider referral to the Mental Health Team, as most treatment is best initiated in secondary care.
- A risk assessment of suicidal ideation should be made. If it is considered that compulsory hospital admission would be in the patient’s interest, the MHA or Common Law may need to be invoked. See separate Compulsory Hospitalisation article for further details.
- Antidepressants may be less effective in bipolar disorder, even if depression is the main feature. They should be used carefully, as they may induce mania or hypomania or rapid cycling. If antidepressants are required then they should be prescribed with anti-manic medication.
- Mild depression may not require any specific therapy and patients should be reviewed initially on a 1- to 2-week basis.
- If depression develops rapidly in a patient with a previous manic episode who is not on treatment then an anti-manic drug should be started (as above).
- Patients with moderate-to-severe depression should be offered fluoxetine combined with olanzapine or quetiapine on its own.
- If there is no response, lamotrigine on its own can be tried.
- If patients are already taking lamotrigine, the level should be checked and the dose increased as necessary. If this fails, fluoxetine combined with olanzapine or quetiapine can be added. The fluoxetine can be omitted if the patient prefers.
- For patients already on valproate, a similar approach should be taken to people who are on lithium.
- Patients may also require psychological therapy.
- Review psychological and pharmacological treatments within four weeks of the acute episode. Options include long-term treatment (in which case review in 3-6 months) or stopping treatment. If treatment is stopped, the patient should be counselled about reporting early symptoms of recurrence.
- Long-term pharmaceutical options may include lithium with or without valproate, or if the patient does not want regular monitoring, various combinations or sole use of valproate, quetiapine and olanzapine.

**Treatment of an acute mixed episode**

- During an acute mixed episode antidepressants should be avoided and the aim should be to try to stabilise patients on anti-manic medication (as above).
Long-term treatment in secondary care to prevent relapse or recurrence

After each acute episode of mania or bipolar depression, a discussion should be had with the patient and/or carer about the nature and course of the disorder, treatment options, the risk of relapse after stopping treatment and the risks and benefits of pharmacological and psychological therapy. Risks may be particularly relevant in women of child-bearing age. Factors to take into account include:

- The severity and frequency of episodes.
- Previous response to therapy.
- Symptoms between episodes.
- Relapse triggers, warning signs of relapse and coping strategies.
- Potential length of treatment and review arrangements.

Provide clear written information about bipolar disorder, including the information for the public from the National Institute for Health and Care Excellence (NICE). Ensure there is enough time to discuss options and concerns.:[1]

Options available include:

- Pharmacological:
  - Lithium should be considered first-line, with the addition of valproate if ineffective.
  - Valproate or olanzapine should be considered for patients intolerant of lithium or who are not prepared to undergo regular monitoring.
  - If symptoms still continue then the patient should be referred to a mental health specialist. Medications that might be used in this situation are lamotrigine (especially in bipolar II disorder) or carbamazepine.
  - Lithium will require monitoring of levels and monitoring of renal function and thyroid function. Patients need to be advised of adequate rehydration and the dangers of suddenly stopping treatment.
  - Long-term therapy usually continues for two years but may be needed for as long as five years.
  - If medication is stopped, patients should be made aware of early warning symptoms of recurrence. Medication should be tailed off gradually (unless acute toxicity develops). Mood should be monitored for two years after treatment is stopped.

- Cognitive behavioural therapy, interpersonal therapy or behavioural couples therapy may be appropriate.
- NICE provides a link to an evidence-based manual to a psychological intervention that has been developed specifically for bipolar disorder.
- Psychosocial education is beneficial. Various methods are available, including teaching coping strategies and managing communication difficulties. [6] Psychosocial interventions are particularly important for paediatric and adolescent patients, to provide families with an understanding of symptoms, course and treatment. [13]

Treatment of rapid cycling [14]

- Year prevalence of rapid cycling among all bipolar patients ranges between 5-33.3%, while lifetime prevalence ranges between 25.8-43%.
- It is associated with a longer course of illness, an earlier age at onset, more illegal drug and alcohol abuse and increased suicidality.
- Patients with rapid cycling should have their thyroid function tested. If they are on antidepressants these should be stopped. Anti-manic therapy should be optimised and compliance checked. First-line therapy is a combination of lithium and valproate and, if this fails, lithium alone can be used.[1] Lithium withdrawal or toxicity may also cause rapid cycling and levels should be checked.
Other treatments\[1\]

- Topiramate and gabapentin are not recommended by NICE.
- Electroconvulsive therapy (ECT): NICE guidelines mention that ECT can provide rapid improvement of symptoms in severe cases of mania if all other options have been unsuccessful. However, the effect is short-lived.
- Transcranial magnetic stimulation: this is not recommended by NICE.

Monitoring patients\[1\]

Once patients begin treatment they should be reviewed at least weekly and then annually once they are stable. Special attention should be paid to lipid levels, plasma glucose, weight, use of tobacco, alcohol and other illicit drugs and monitoring of blood pressure. Regular questioning about side-effects and suicidal ideation should occur.

Mania in special groups\[1\]

Children and adolescents

The diagnosis of mania in young patients is similar to that for adults but mania must be present. Another feature which makes the diagnosis is euphoria present on most days. Irritability may aid the diagnosis but is not necessary. The treatment in children and adolescents is essentially the same as in adults but should be initiated under mental health specialists. Aripiprazole has been recommended for moderate-to-severe manic episodes in adolescents with bipolar I disorder for up to 12 weeks in adolescents aged 13 and older.\[15\]

Pregnancy

Medications used for mania in child-bearing women may have an impact on the fetus if they become pregnant. Therefore, thorough advice about contraception and the risks of becoming pregnant must be discussed.\[2\] Drugs, such as carbamazepine, valproate and lamotrigine, have to be stopped if patients become pregnant.\[16\]

No specific anti-manic medication is licensed in pregnancy. If a pregnant women develops mania then low doses of antipsychotics can be used.

Elderly

Bipolar disorder may present in elderly patients. Disorders, such as cerebrovascular accidents and thyroid disorders, need to be excluded. Older patients should be treated as above. Older patients are more likely to develop sudden depression after recovery from a manic episode and need close follow-up. Elderly patients are also more likely to develop side-effects and have drug interactions.

Prognosis\[1\]

- Bipolar disorder is a chronic, lifelong illness.
- On average, ten episodes are experienced in a lifetime.
- The risk of recurrence is high. In the twelve months after a mood episode, the recurrence rate is 50% at one year, 75% at four years and 10% thereafter.
- The pattern of remissions and relapses is very variable. The symptom-free period tends to become shorter as time goes by and depressive episodes become more frequent and longer-lasting.
- There is a high lifetime suicide risk in patients with bipolar disorder. 25-56% present at least one suicide attempt during their lifetime and 15-19% die from the attempt.\[17\] Lithium has been shown to reduce the risk of suicide and the number of suicide attempts in bipolar disorder.\[18\]

Further reading & references

- Valproate - patient guide; Booklet for a girl or a woman taking any medicine containing valproate, with key information about the risks of valproate in pregnancy; (Jan 2016)
1. Bipolar disorder - the assessment and management of bipolar disorder in adults children and young people in primary and secondary care; NICE Clinical Guideline (Sept 2014, updated 2016)
2. Evidence-based guidelines for treating bipolar disorder: revised second edition; British Association for Psychopharmacology (March 2009)
5. Management of Bipolar Disorder in Adults, Children and Adolescents in Primary and Secondary Care; Royal College of Psychiatrists Publication, 2006
8. The ICD-10 Classification of Mental and Behavioural Disorders; World Health Organization
15. Aripiprazole for treating moderate to severe manic episodes in adolescents with bipolar I disorder; NICE Technology Appraisal Guidance, July 2013
16. Antenatal and postnatal mental health: clinical management and service guidance; NICE Clinical Guideline (December 2014)

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