Bipolar disorder
Focus on mania

An episode of acute mania is a medical emergency. The GP can play a pivotal role in its early identification and prevention, and may need to initiate treatment if there are limited local mental health services.

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In Australia, bipolar disorder afflicts 1.3% of the population at some stage of their life, and 0.9% in any 12-month period.[1] The peak onset of illness is usually in early adult life (late adolescence to late 20s) and there is a strong genetic basis.

The impact of bipolar disorder on affected individuals, and those close to them, is profound; this is the sixth most disabling condition across the whole of medicine.[2] Disrupted relationships are common, rates of unemployment are high (at the least, achievement of career aspirations may be significantly hampered) and many are forced onto government benefits. Furthermore, mortality rates are substantially increased, mainly due to higher rates of cardiovascular and cerebrovascular disease, diabetes and obesity.[3] At least a quarter of affected individuals will attempt suicide on one or more occasions, and at over 100 cases per 100,000 person years, suicide rates are greatly increased compared with the general population.[4]

The marked disability and mortality in individuals with bipolar disorder mean that GPs need to be on the alert for early diagnosis and the implementation of an appropriate ongoing management strategy. As bipolar disorder usually initially presents in late adolescence or early adulthood, the potential for long-lasting damage to many aspects of day-to-day functioning is profound. For

IN SUMMARY

- **An episode of acute mania is a medical emergency. Insight and judgement are usually impaired early and urgent involuntary hospitalisation under the relevant mental health legislation is frequently required to protect the patient.**
- **GPs have an important role in early identification and prevention of mania, and may need to initiate treatment if there are limited local mental health services.**
- **The two components of the pharmacological management of acute mania are primary treatment of the pathologically elevated mood and short-term containment of any associated behavioural disturbance such as aggression or violence, agitation or overactivity, and disinhibition.**
- **Primary treatment of the pathologically elevated mood is with lithium, sodium valproate, carbamazepine or a second-generation antipsychotic. This treatment will usually be continued for prophylaxis.**
- **Short-term containment of associated behavioural disturbance comprises calming or sedating the patient until their mood stabilises, and usually involves temporary use of supplementary antipsychotics or benzodiazepines.**
- **Psychological therapies have a critical role in preventing relapse into mania and stopping mild elevations of mood progressing to full manic presentations.**

Table 1. Features of mania, hypomania and mixed episodes

Mania

- Excessively elevated or euphoric and/or irritable mood
- Duration of at least one week
- Characteristic symptoms and behavioural change:
  - inflated sense of own abilities/ capabilities (grandiosity)
  - disinhibition – may manifest as increased libido, increased spending, overly frank comments about others, impaired judgement in work or relationships
  - increased speed of thoughts, increasingly talkative (perhaps associated with 'flight of ideas')
  - increased activity levels and increased subjective energy (occasionally associated with physical agitation)
  - lack of focus, distractibility
  - reduced need for sleep
- Evidence of marked impairment in functioning, with or without psychotic features (delusions, hallucinations), and possibly with hospitalisation

Hypomania

- Excessively elevated or euphoric and/or irritable mood – same as in mania
- Duration of at least two to four days – shorter than in mania
- Characteristic symptoms and behavioural change – same as in mania
- Mood and behaviour distinctly different to normal, but not severely impairing and no psychotic features or hospitalisation – less extreme than in mania

Mixed episodes

- Presentations characterised by concurrent presence of manic or hypomanic symptoms and depressive symptoms
- Usually the manic or hypomanic features predominate
- Sometimes referred to as 'dysphoric mania'

the vast majority of patients, this is a highly recurrent condition.

There is a welcome and increasing interest in shared care between the primary and secondary care sectors for patients with mental health conditions. The authors suggest that a psychiatrist should assess most patients with bipolar disorder at least once, early in the course of their treatment program, with recommendations being made for appropriate pharmacological and psychological treatments. Bipolar disorder is a complex mental illness and, unlike with conditions such as depression, anxiety and substance use, the average GP would treat relatively few patients with bipolar disorder over a professional career.

For those patients with severe and/or markedly recurrent illness, ongoing care is probably best managed in the mental health sector. Those patients with either less severe or very treatment-responsive illness are probably best managed primarily by the GP, with the psychiatrist providing occasional clinical review and 'back-up' when complications or major recurrences occur. However, an episode of acute mania is a medical emergency and requires urgent referral to a psychiatrist and/or community mental health team.

Patients with bipolar disorder may have periods of mania or hypomania and periods of bipolar depression or may have depressive symptoms intertwined with the mania ('mixed episode' or 'dysphoric mania'). The illness is usually categorised into bipolar I and bipolar II types: bipolar I disorder is diagnosed if the patient has had at least one episode of mania, and bipolar II disorder if there have only been hypomanic and depressive episodes. Comorbidity with substance dependence or abuse is common, occurring in about 50% of subjects.

This first article of a series on the management of bipolar disorder focuses on the management of mania. The general principles for managing mania, the medications approved for this presentation and psychological treatments developed for use early in the manic process to prevent relapse are described. Other articles will cover the management of depression, the distinguishing of bipolar depression from unipolar depression and maintenance therapy for bipolar disorder.

Clinical features and diagnosis

The clinical features of mania are elevated, expansive or irritable mood, accelerated speech, racing thoughts with flight of ideas, increased activity and reduced need for sleep. Patients may develop grandiose ideas, act recklessly (including increased spending) and show increased sexual drive and activity. Symptoms often appear abruptly. Where symptoms are less severe and of shorter duration, the term 'hypomania' is used. The clinical features of mania, hypomania and mixed episodes, based on the formal *DSM-IV-TR* criteria, are compared in Table 1, and broad 'clinical clues' for identifying patients in the manic or hypomanic phase of bipolar disorder are listed in Table 2.

For patients with a first presentation of mania, particularly when the initial onset occurs after the age of 40 years, organic causes such as medications (e.g. corticosteroids or dopaminergic agents for Parkinson's disease), endocrine disorders (e.g. hyperthyroidism) or neurological conditions (e.g. frontal lobe tumours or cerebrovascular disease) should be excluded. In practice, however, such organic aetiologies are very uncommon. In younger first presentations, psychiatric

Table 2. Clinical clues for identifying mania and hypomania[7]

Symptoms and signs include the following behaviours if out of character for the individual:

- Feeling energised and 'wired'
- Excessively seeking stimulation
- Overly driven in pursuit of goals
- Needing less sleep
- Irritable if stopped from carrying out ideas
- Disinhibited and flirtatious
- Offensive or insensitive to the needs of others
- Spending money in an unusual manner or inappropriately
- Indiscreet and disregarding social boundaries
- Having poor self-regulation
- Making excessively creative and grandiose plans
- Having difficulty discussing issues rationally or maturely
- Reporting enhanced sensory experiences

differential diagnoses include schizophrenia, schizoaffective disorder and substance abuse.

General principles in the management of mania

An episode of acute mania is a medical emergency. Patients have the capacity to destroy their reputations, relationships and finances within hours or days. Insight and judgement are usually impaired early, even in the absence of delusions, and urgent involuntary hospitalisation under the relevant mental health legislation is frequently required to protect the patient. However, the decision to admit may be traumatic for the patient and family members, all of whom will need support.

If community or outpatient treatment occurs, it is essential to monitor risky behaviour, such as financial indiscretion or potential harm to others, such as from hazardous driving. A financial power of attorney may be necessary. Outpatient attendance is often erratic, and a legally enforceable community treatment order may be required.

It has been said that patients with acute mania are 'always worse than they seem'. An apparently reasonable level of function during a brief assessment may mask more serious dysfunction. Reports from family and friends should be taken seriously, but interpreted with an understanding of the patient's normal function and the nature of these relationships. Irrespective of whether inpatient or community treatment is required, the occurrence of mania will require urgent referral to a psychiatrist and/or community mental health team.

Manic relapses in patients with established bipolar disorder are often due to poor medication adherence, so serum concentrations of medications should be checked where this is relevant. Other common causes of relapse include substance abuse (particularly that involving cannabis, cocaine or amphetamines), use of antidepressants and stressful life events. If the patient is taking an antidepressant, this should be ceased.

Medications

The two components of the pharmacological management of acute mania are primary treatment of the pathologically elevated mood and short-term containment of any associated behavioural disturbance such as aggression or violence, agitation or overactivity, and disinhibition (see the box on this page).[5]

Primary treatment of the pathologically elevated mood involves the commencement of lithium, sodium valproate, carbamazepine or a second-generation antipsychotic. There is usually a delay of effect of one to two weeks, although some improvement often occurs within the first few days. This treatment will usually be continued for prophylaxis.

Principles of medication treatment of acute mania and hypomania[5]

Primary treatment of the pathologically elevated mood

The following medications are used as mood stabilisers:

- Lithium
- Anticonvulsants: sodium valproate, carbamazepine
- Second-generation antipsychotics: aripiprazole, olanzapine, quetiapine, risperidone, ziprasidone

Short-term containment of any associated behavioural disturbance

The following medications are used until the mood becomes stabilised:

- Supplemental antipsychotics (first- or second-generation) – if not already chosen as a mood stabiliser
- Supplemental benzodiazepines

Short-term containment of any associated behavioural disturbance comprises calming or sedating the patient as an interim measure until his or her mood stabilises. It usually involves the temporary use of supplementary antipsychotics (first- or second-generation) or benzodiazepines (e.g. diazepam or clonazepam). The aim should be to gradually withdraw these once the mania settles.

The medications demonstrated to be of value in the acute management of mania are listed in Table 3, and the current status of TGA approval and PBS listing for the treatment of acute mania for these drugs is given in Table 4. Further details on pharmacological options can be obtained from the Royal Australian and New Zealand College of Psychiatrists' clinical practice guidelines for the treatment of bipolar disorder (*Bipolar Disorder Clinical Version*, available in pdf format from http://www.ranzcp.org/resources/clinical-practice-guidelines.html)

continued

Table 3. Medications demonstrated to be effective in the acute treatment of mania*

Mood stabiliser
- Lithium

Anticonvulsants
- Sodium valproate
- Carbamazepine

First-generation antipsychotics
- Chlorpromazine
- Haloperidol

Second-generation antipsychotics
- Aripiprazole
- Olanzapine
- Quetiapine
- Risperidone
- Ziprasidone

* Demonstrated to be effective in randomised controlled trials.

Table 4. TGA and PBS status of medications demonstrated to be effective in acute mania

Drug effective in acute mania*	TGA approved for acute mania	PBS listed for acute mania
Mood stabiliser		
Lithium	Yes	Yes
Anticonvulsants (used to stabilise mood)		
Sodium valproate	Yes	Yes
Carbamazepine	Yes	Yes
First–generation antipsychotics		
Chlorpromazine	Yes	Yes
Haloperidol	Yes	Yes
Second-generation antipsychotics		
Aripiprazole	No	No
Olanzapine	Yes (monotherapy or adjunctive therapy)	No
Quetiapine	Yes (monotherapy or adjunctive therapy)	Yes (monotherapy)
Risperidone	Yes	Yes (adjunctive therapy)
Ziprasidone	Yes (monotherapy, mixed episodes)	Yes (monotherapy, mixed episodes)

* Demonstrated to be effective in randomised controlled trials.

or *Therapeutic Guidelines: Psychotropic*, Version 6.[5,6]

Psychological therapies

There is growing evidence for the benefits of psychological therapies in bipolar disorder. These treatments play a critical role (in conjunction with medications) in either preventing relapse into mania or stopping mild elevations of mood progressing to full manic presentations. However, they are not useful once the patient is in the full manic episode.

Psychological therapies shown to be useful in this role include:[7]

- education about the condition and its treatment
- cognitive behavioural techniques – for example, identifying triggers and planning how to minimise or avoid them, accurately labelling emotions, identifying thoughts and reframing them into more positive rational responses, and dealing with adjustment/self-esteem issues and long-term vulnerabilities
- interpersonal and social rhythms therapy – teaches patients to be more effective in handling relationships and make graded lifestyle changes to increase stability, and highlights the importance of routine and sleep
- schema-focused cognitive therapy – this is a more lengthy process necessary for some patients whose core beliefs are embedded in feelings of inadequacy, failure or unrelenting standards that continue to drive self-defeating behaviours
- mindfulness meditation
- supportive psychotherapy – this is particularly useful in identifying interpersonal triggers that affect the patient's mood, and may include problem-solving approaches; it is most useful in the maintenance stage of treatment, once the skills of cognitive behavioural therapy have been learned
- exercise, yoga, relaxation therapy and similar 'mind–body' interventions individualised to the needs and lifestyle of the patient (these may also be beneficial in the maintenance stage).

Specific issues for management in the general practice setting

Identification of early warning signs to prevent relapse

Some patients switch into mania rapidly and without warning, losing insight

Table 5. Early warning signs for manic relapse – the relapse profile[7]

- Increasing activities and busyness
- Reduced need for sleep
- Impulsive behaviour
- Speaking in a caustic manner
- Telephoning friends indiscriminately

quickly. A considerable proportion, however, have a 'transitional' phase with early warning signs that begin hours, days or weeks prior to the onset of frank manic symptoms. (Interestingly, early warning signs rarely occur prior to the development of a bipolar depressive episode). With training, both the patient and his or her family can often identify the behaviour changes in this transitional phase.

Common early warning signs are insomnia, a reduced need for sleep, increased energy and irritability. If such signs can be reliably identified, counteracting strategies can be developed. For example, behavioural means of improving sleep can be instituted, associated stresses (such as relationship or work difficulties) addressed, or medications such as hypnotics or antipsychotics commenced with the intent of aborting progression to a full manic episode. As the GP has a greater awareness of the day-to-day clinical status and life context of the patient, he or she is often in a better situation than the specialist to identify and deal with such early signs.

Other techniques such as the patient completing daily mood charts may assist in identifying early features of a 'slide' into a manic or depressive relapse. Active collaboration with a skilled psychologist will help the GP in designing and carrying out such interventions. More details on identifying these 'early warning signs' and on strategies for preventing progression into a manic relapse are detailed in Tables 5 and 6. Guidance on when to refer the patient to psychological services is provided in Table 7.

There are now a large number of quality information sources on this condition for patients, families and friends, some of which are detailed in the box on page 50.

Confidentiality during mania or hypomania

An issue central to the nature of bipolar disorder is the loss of insight during the course of mania or hypomania. It should be noted that some patients rarely lose insight during hypomania.

The GP must consider as paramount the ongoing welfare of patients as behaviour may be markedly disturbed during episodes. Patients may engage in behaviour with severe future ramifications, such as embarking upon unwise business schemes, spending large amounts of money or becoming aggressive with a real potential of physical harm to others. Despite the patient's protestations at the time, it is imperative for the clinician to intervene in such situations, although this may arouse considerable patient anger or irritation.

It may be necessary to invoke local mental health act legislation to enforce treatment. Sometimes, however, the patient will reluctantly comply with the instructions of the clinician and/or family to avoid involuntary treatment; such a response is more likely where strong prior trust in the doctor–patient relationship has been nurtured. The GP should always be aware that the patient's behaviour in the surgery might appear more normal than that actually occurring in his or her day-to-day life. As a general principle, an account of disturbed or disrupted behaviour by a sensible friend or relative should always be taken seriously if it conflicts with the claims of the patient with mania.

A related and complex issue is what should be communicated to the patient's

Table 6. Strategies for patients to prevent progression into a manic relapse[7]

- Establish a regular routine for eating and sleeping
- Minimise sleep disruption and other stressors and triggers
- Spend nights in your bedroom even if you are not sleeping — lie down and rest as much as you can
- Prioritise and reduce the number of tasks you are involved in
- Modify excessive behaviour — slow down
- Engage in calming activities and be aware of how you are thinking, feeling and behaving
- Carefully follow through the consequences of your actions — consider the costs and benefits
- Delay impulsive actions — if it is still a good idea in a few days time, it might really be a good idea
- Spend time on your own to reduce stimulation, for example by avoiding crowds, busy shops, intense movies and parties
- Find a quiet, restful place to pass the time
- Keep a diary of your moods and reactions
- Reframe your overly inflated thoughts as symptoms
- Recognise if you are getting into destructive situations
- Talk to someone you can trust
- Avoid drinking tea, coffee, cola and other drinks that contain caffeine
- Avoid alcohol, marijuana and other drugs
- See a doctor to review your medications and current state

Table 7. When to refer patients with mania to psychological services[7]

- Patient is having difficulty understanding or accepting the diagnosis
- Medication adherence is less than optimal
- Relapses occur, suggesting the need for symptom management skills to supplement medication
- Patient has unresolved issues or trauma resulting from the phase of the illness or hospitalisation
- Patient has difficulty in adjusting to relationships or work
- Cognitive distortions act to destabilise mood
- Patient has difficulty identifying stressors or triggers leading to relapse
- Patient has sustained feelings of loss of direction or meaning
- Personality difficulties hinder recovery

Table 8. Recommended physical monitoring and testing of patients with bipolar disorder taking mood stabilisers

Monitoring of all patients

At least once a year:*

- Lipid levels, including cholesterol, in patients aged over 40 years
- Plasma glucose levels
- Weight
- Smoking status and alcohol use
- Blood pressure

Monitoring for specific drugs

Lithium

- Serum lithium concentrations – every three to six months for patients on regular dosage; aim for 0.6 to 0.8 mmol/L
- TSH and electrolytes/urea/creatinine/eGFR – every six to 12 months; to exclude hypothyroidism or declining renal function

Carbamazepine

- Serum carbamazepine concentrations – every three to six months; aim for 17 to 50 micromol/L
- Liver function tests – every three to six months; to exclude hepatotoxicity
- Full blood count – every three to six months; to exclude aplastic anaemia and other haematological dyscrasias
- Electrolytes – every three to six months; to exclude hyponatraemia

Sodium valproate

- Serum sodium valproate concentrations – every three months; aim for 300 to 700 micromol/L
- Liver function tests – every three to six months; to exclude hepatotoxicity
- Full blood count – every three to six months; to exclude thrombocytopenia

Second-generation antipsychotics

- Blood sugar levels and serum lipids – every six months; to exclude diabetes and hyperlipidaemias

* As recommended by the UK National Institute of Health and Clinical Excellence[8]

ABBREVIATIONS: eGFR = estimated glomerular filtration rate; TSH = thyroid-stimulating hormone.

family if the manic patient refuses contact with them, or when family members attempt to speak to the practitioner without the patient's approval or awareness. In traditional health legislation, the rights of the patient to privacy are given primacy in these situations. The authors would contend, however, that respect of such 'rights' may not always be appropriate, or in the patient's long-term interest – particularly when the patient lives with the family or the family has ongoing financial or other responsibilities. In such situations, it may be more appropriate to consider the whole family context as 'the patient'. It would, therefore, be wise for clinicians to inform patients early in their contact that if their behaviour is destructive to themselves or others, practitioners involved in their management and family members may need to be notified without their consent if necessary. On the other hand, for those who have been estranged from family for prolonged periods when well, such engagement of the family during illness may be inappropriate. Recognition of the necessity to involve designated 'primary care givers' has been formalised under some state mental health legislations. (Note that mental health legislation differs from state to state).

For those patients who are prone to spending or borrowing large amounts of money during manic episodes, serious consideration should be given to strategies such as:

- arranging for a power-of-attorney by a family member
- using relevant state bodies to take over the patient's financial affairs
- simple actions for reducing ease of spending large amounts of money such as encouraging the patient to give up the use of credit cards.

Monitoring of physical status and medications

In view of the recent recognition of premature mortality in the bipolar disorder population, largely due to cardiovascular and cerebrovascular disease, the physical status of patients should be monitored regularly (at least annually).

Particular attention should be given to monitoring lipid and glucose levels, as well as weight, smoking status, alcohol use and exercise participation, as listed in Table 8.[8]

Sources of information on bipolar disorder for patients, families and friends

Books

Berk L, Berk M, Castle D, Lauder S. Living with bipolar: a guide to understanding and managing the disorder. Sydney: Allen & Unwin; 2008.

Eyers K, Parker G. Mastering bipolar disorder: an insider's guide to managing mood swings and finding balance. Sydney: Allen & Unwin; 2008.

Rowe P, Rowe J. The best of times, the worst of times: our family's journey with bipolar. Sydney: Allen & Unwin; 2005.

Russell S. A lifelong journey: staying well with manic–depression/bipolar disorder. Melbourne: Michelle Anderson Publishing; 2005.

DVDs

Manic–depressive illness: a guide to living with it. Monkey See Productions (http://www.monkeysee.com.au).

Troubled minds: the lithium revolution. SBS Productions/Film Australia. (Available for purchase by educational institutions from Enhance TV, at www.enhancetv.com.au).

Websites

Beyondblue: The National Depression Initiative – http://www.beyondblue.org.au

Black Dog Institute – http://www.blackdoginstitute.org.au

Recommendations on the frequency of blood monitoring for patients on the various mood stabilising medications are also detailed in this table.

Conclusion

Mania is a medical emergency with drastic consequences for the patient and family if poorly managed. The GP can play a pivotal role in early identification and prevention of the condition and may need to initiate treatment if there are limited local mental health services. MT

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Further reading

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Joyce PR, Mitchell PB, eds. Mood disorders: recognition and treatment. Sydney: UNSW Press; 2005.

COMPETING INTERESTS: In the past three years, Professor Mitchell has received remuneration for advisory board membership from Eli Lilly and AstraZeneca; and consultative fees or lecture honoraria from AstraZeneca, Eli Lilly, Janssen-Cilag and Lundbeck. He is not currently a member of any pharmaceutical company advisory board. Dr Ball and Dr Gould: None.