MedicineToday

The Peer Reviewed Journal of Clinical Practice

Making sense of the complex depressed patient

Reprint Collection

Part 1: medical illness, including effects of drugs and alcohol

Part 2: temperament and personality factors

Part 3: melancholic and psychotic depression

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MedicineToday PEER REVIEWED ARTICLE

MedicineToday 2009; 10(4): 36-46

Making sense of the complex depressed patient

Part 1: medical illness, including effects of drugs and alcohol

Depression takes various forms in people with medical illness including normal experience, personality traits, adjustment reactions/disorders and clinical disorders. Differing approaches are required to treat these and enhance the patient's ability to cope with the medical illness and other comorbidities.

KAY WILHELM
AM, MB BS, MD, FRANZCP

Professor Wilhelm is Conjoint Professor, School of Psychiatry, University of NSW, and Senior Staff Specialist, Consultation–Liaison Psychiatry, St Vincent's Hospital, Sydney, NSW.

Depression is viewed as a major public health challenge for the twenty-first century and there has been considerable 'consciousness raising' over the past decade. Depression is now seen as often fitting a chronic disease model and there are many factors that complicate presentation and course.

Analysis of data from the National Survey of Mental Health and Well-being carried out in 1997 shows current (30-day) prevalence rates of major depression of 3.2% in Australia, with unemployment and smoking status, presence and number of medical illnesses, followed by being in midlife, previously married and female all as independent risk factors.[1] There are higher rates of depression in the presence of respiratory disease, cardiovascular and vascular disease, Parkinson's disease, diabetes, renal disease, cancers, HIV infection, smoking, alcohol use and illicit drug use.[1,2]

Depression may take many forms, particularly in people with a medical illness, and its manifestation is influenced by the patient's temperament and personality style. The depression may become chronic, and can be part of bipolar disorder. This

IN SUMMARY

- Depression in the context of medical illness is often viewed as being 'understandable' and not requiring treatment. However, the physical illness and its treatment can contribute to the precipitation of clinical depression.
- Psychotherapy and allied health interventions (including clinical psychology, occupational therapy and physiotherapy) should be considered as well as antidepressants when managing depression in patients with medical illnesses.
- When choosing medications, the target symptoms and the side effect profiles of the medications should be considered.
- Dual action antidepressants, which are both serotonergic and noradrenergic, can improve depression, insomnia and pain tolerance.
- In those patients with multiple medical, psychiatric and substance use comorbidities, ceasing substance use can assist mental as well as physical health.

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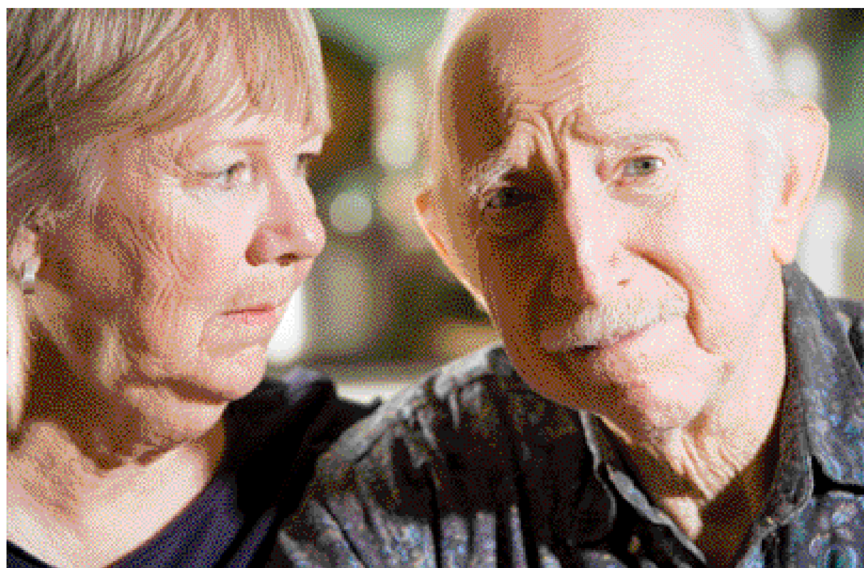

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article, the first of three in this supplement on the complex depressed patient, discusses the types of depression seen in people with a medical illness and also approaches to management. The other articles discuss the influence of patients' temperamental and personality factors on the choice of management and the likely problems, and the assessment and management of patients with melancholic depression, including those with bipolar disorder.

Depression and medical illness

Depression in patients with a medical illness can take the form of 'normal' reactive depressive symptoms, including demoralisation and grief.[3] However, there can be interactions between physical illness and depression, including symptoms being shared between depression and medical illness (for example, tiredness, anorexia and insomnia) and depression arising as a prodrome to, or consequence of, the medical illness. Many serious medical illnesses are accompanied by some depressive symptoms, and some medical illnesses (including malignancy, painful syndromes, endocrine disorders and some viral disorders) and some medications are depressogenic, although this effect may be masked by somatising behaviour.[4] Illnesses and medications that may lead to depression are listed in Table 1. Fact sheets for patients about depression in a variety of medical illnesses are available on the beyondblue website (see the box on page 6).

Table 1. Illnesses and medications leading to depression[3]

Neurological and intracerebral illnesses
- Small and large vessel cerebrovascular disease
- Stroke
- Arteriovenous malformations
- Parkinson's disease
- Huntington's disease
- Tumours
- Autoimmune disease (e.g. systemic lupus erythematosus), especially those leading to cerebral vasculitis
- Early dementia from any cause

Occult neoplasms
- Abdominal cancers particularly (e.g. pancreatic cancer)
- Small cell carcinoma of lung
- Tumours in frontal lobes

Medications*
- Antihypertensives
- Beta blockers
- Cimetidine
- Corticosteroids
- Oral contraceptives
- Interferon
- Isotretinoin
- Vinblastine
- Vincristine
- Most tranquillisers, sedatives and antipsychotic drugs
- Anti-inflammatory agents

Substance abuse
- Amphetamines/cocaine
- Other stimulant dependence
- Nicotine dependence
- Alcohol abuse and dependence
- Sedative abuse and dependence

Infections
- Cerebral infection (bacterial or viral)

Endocrine disorders
- Addison's disease
- Cushing's syndrome
- Thyroid disease
- Diabetes (type 1 and type 2)

Cardiac, respiratory, renal illnesses
- Heart failure
- Myocardial infarct
- Chronic respiratory disease
- Renal failure

* Not a comprehensive list

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There is also a 'vicious cycle' whereby depression is associated with worsening of the index medical illness, with greater morbidity in turn leading to increased severity of depression. Suicidal ideation occurs generally in medically ill patients who also fulfil criteria for major depression, and often diminishes or disappears with assertive treatment of the depressive disorder.

Clearly substance abuse and personality factors also play a part. Dependent users of nicotine and alcohol have higher rates of depression, and many of the common depressogenic medical illnesses and nicotine and/or alcohol use adversely affect each other. Dependent smokers have higher rates of suicidal ideation than nonsmokers, and these rates increase with the number of cigarettes smoked (smokers of 25 or more cigarettes a day have four times the rates of suicidal ideation of nonsmokers).[5] Compounding factors include the effects of abuse of, dependence on and withdrawal from alcohol, cannabis, nicotine, cocaine, amphetamines and other recreational drugs, the effects of analgesics and sedative/hypnotic drugs, and the side effects of medications, particularly in the context of multiple medications.

Two parallel agendas

Type and severity of depression

The type and severity of the depression need to be determined. The comment, 'of course the patient is feeling like that when they're so ill', is often heard. Additionally, depression may be masked by somatising behaviour[4] and some disorders can mimic depression (including hypoactive delirium and frontal dementia). Although is it normal for people to feel sad and distressed about the prospect of dealing with a serious medical illness, pointers to clinical depression in such people include their feeling consistently depressed and having lack of reactivity, lowered self-esteem and increased self-blame, hopelessness and rumination (stewing over things).[6]

Some criteria for major depression (such as changes in sleep, appetite and concentration) are less discriminating in the presence of any of the many medical illnesses where they are also common features.[6,7] As a rule of thumb, when patients become depressed, they experience lowered self-esteem and increased self-criticism, guilty thoughts and tendency to ruminate or stew, and become preoccupied with hopelessness. They may develop psychomotor changes (indicative of melancholic depression) and may even become psychotic. These features do not occur in nondepressed people with medical illness, who may still be fatigued and experience appetite or sleep disturbance, demoralisation, grief and medical or medication complications due to their medical condition.

It is often possible to distinguish between depressed and nondepressed patients with medical illness. The DMI-10 (10-item Depression in the Mentally Ill Scale) or 12-item SPHERE (Somatic and Psychological Health Report) plus a disability measure such as the SF-12 (the Short-Form 12-Item Health Survey) can be helpful here.[6-8] The version of SPHERE on the beyondblue website also has behavioural items indicating disability (see page 6). In cases where there is doubt, the judicious trial of an antidepressant is appropriate. An information sheet for GPs about antidepressant drug prescription is available on the Black Dog Institute website (see the box on page 6).

Complicating illnesses and medications

The other agenda is consider the presence of a range of medical illnesses and their treatments that can complicate the course of depression by precipitating onset, prolonging course, affecting impact of antidepressants and mimicking depression (Table 2).

People with histories of substance abuse or dependence are likely to have further complications of both their medical condition and any depression. Such histories include nicotine dependence or abuse, and dependence on alcohol, prescribed or illicit drugs (including sedatives/hypnotics, stimulants and other psychoactive agents).

Table 2. Factors complicating depression in patients with medical illness

- A wide range of illnesses cause symptoms or signs that precipitate depressive symptoms (see Table 1); some also mimic depression (e.g. organ failure, frontal lobe disease, hypothyroidism, Parkinson's disease)
- Comorbid alcohol/substance/ analgesic/sedative abuse or dependence, nicotine dependence
- Presence of delirium (especially hypoactive delirium) and/or dementia
- Medications that precipitate, mimic or mask depression or interact with psychoactive medications
- 'Unfinished emotional business', especially grief and anger
- Underlying personality traits, personality disorder
- Presence of anxiety disorders and somatising behaviour
- Side effects of prescribed medications and interactions between medications used to treat medical illness

Assessing a patient with melancholic depression

As later onset melancholic major depression is associated with cerebrovascular disease, there are likely to be increased rates of melancholic depression in people with medical illnesses predisposing to vascular disease, Parkinson's disease and some malignancies. An information sheet for GPs about melancholic depression is available on the Black Dog Institute website (see page 6). (The third article in this series will discuss melancholic depression in more depth.)

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continued

Table 3. Assessing depression in patients with medical illness

Patient feature	Assessment
Does the patient have an anxiety and/or depressive disorder?	Exclude delirium, changes due to medical illness, intoxication – self-report instruments such as DMI-10 and SPHERE can assist in identification of depression types[6,7] Exclude delirium and dementia, especially frontal dementia, as both can be interpreted as depression Check orientation, ask relatives about recent behaviour, ask patient to draw clock face, frontal lobe testing
What type of anxiety?	Check whether anxiety is episodic or part of a personality style, and whether it predated the illness
Is there a past history of depression? Is this episode similar to previous episodes?	Consider gathering other details
Is there a history of regular use of nicotine, alcohol or other substances?	Assess history and degree of reliance on these substances – all may affect depression
Have there been any changes in medication leading to drug interactions? Are there increased side effects?	Check drug interactions (consult pharmacist or clinical pharmacologist), treat as appropriate
What sort of sleep problems are there? Is there sleep apnoea?	Consider sleep hygiene, assess and treat sleep apnoea
Is there evidence of malabsorption or dietary problems?	Dietary problems will resolve when malabsorption is treated May lead to vitamin B_{12} and/or folate deficiency
Is there significant pain?	Pain is a potent source of inactivity and helplessness and can be a powerful precipitant of depressive episodes Pain and analgesics can maintain depression
Is there evidence of somatising behaviour?	Consider what is being communicated by the behaviour

The following questions can be useful in identifying the symptoms of melancholic depression:[9]

- Are you stewing over things?
- Do you still read the newspaper or watch TV?
- How do you spend your day?
- Do you still enjoy hobbies/children/grandchildren?
- Do you feel worse in the morning?
- How do you sleep?
- Do you wake early in the morning?
- Can you be cheered up?
- What lifts your mood?

The characteristic 'psychomotor signs' of melancholic depression of physical and mental agitation and slowing and the associated cognitive changes can be affected by some medical illness but are usually still recognisable. Again, if in doubt, an antidepressant can be trialled. A guide to determining the appropriate assessment of depression in patients with medical illness is given in Table 3.

Management of depression in the medically ill

It is important to consider psychological interventions and physiotherapy as well as the use of antidepressants when managing depression in patients with medical illness. A guide to determining the appropriate intervention is given in Table 4.

Patient-centred counselling

Patients with a medical illness and depression are often frightened and overwhelmed by the combination of physical and emotional factors. They may also be dealing with a series of clinicians. It is important to help them streamline the process, learn to self-manage, ask for help and work collaboratively with the medical teams.

It is necessary to be aware of and understand the meaning of the illness to the patient and to provide counselling for the issues that arise. Patients often feel trapped, immobilised, hopeless and helpless – all these feelings are potent in precipitating and maintaining depressive episodes and may reawaken memories from similar situations in the past. Patients with these emotions will benefit from counselling and support. There may also be 'unfinished business', especially involving suppressed grief and anger, which is

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Table 4. Managing depression in patients with medical illness

Patient feature	Intervention
Is there an unresolved loss?	Consider grief counselling or psychotherapy
Are there current stressors precipitating depression or impeding recovery?	Offer stress management skills, relaxation skills, problem solving, CBT approaches, family support
Is there new anxiety/panic due to breathlessness?	Use specific techniques to improve posture and breathing control, sleep quality, overcome panic
Is there decreased mobility?	Techniques to improve mobility using a rehabilitation framework can be useful; may involve physiotherapy and occupational therapy
Are there long-term interpersonal difficulties?	Identify problems, offer interpersonal, relationship and family therapy where needed; longer term psychotherapy may be required
Are there issues of self-blame about the patient's illness?	Clarify misunderstandings, guilt issues, 'unfinished psychological business'
Are there ongoing undue concerns with health? Is there somatising behaviour? Is there a long history of health anxiety or is it recent?	Use reattribution techniques to illustrate relation between psychological issues and body function[4] Consider CBT for longstanding problems[2]
Use of antidepressants	
Which antidepressant to use?	Consider target symptoms, past history, risk of overdose, medical history, current medications and past sensitivities and interactions
Is there worrying, ruminations, obsessional thinking or rituals?	Consider using an SSRI (generally sertraline, citalopram and escitalopram have the least interactions with other medications and are the best tolerated) or an SNRI (desvenlafaxine, duloxetine or venlafaxine); start low, increase slowly to avoid side effects, which may be more prominent in the medically ill*
Is there fatigue?	Consider using a more stimulating antidepressant (e.g. reboxetine, an SSRI or moclobemide)*
Are there melancholic features?	Use a broad-spectrum antidepressant (e.g. mirtazapine starting at 15 mg, or nortriptyline starting at 10 to 20 mg); an antipsychotic may also be required Patients with little or partial response may require augmentation with mood stabilisers and other medications or ECT, in consultation with a psychiatrist*
Is there significant anxiety or insomnia?	Use a more sedating antidepressant: mirtazapine 15 mg can be helpful for both anxiety and insomnia Bupropion and some TCAs (e.g. small doses of nortriptyline, doxepin) may assist with substance withdrawal*
Is there significant pain?	Consider treating pain with CBT, mindfulness, physical measures (such as massage and stretching) Some antidepressants (e.g. TCAs and mirtazapine) potentiate analgesics; of the TCAs, amitriptyline is particularly useful for pain and depression, while others (e.g. nortriptyline) may have less anticholinergic side effects
Is the patient on other medications for medical illnesses?	Consider using an SSRI (sertraline, citalopram, escitalopram) or mirtazapine, which have the least interactions with other medications; consider on a case by case basis*

ABBREVIATIONS: CBT = cognitive behavioural therapy; ECT = electroconvulsive therapy; SSRI = selective serotonin reuptake inhibitor; SNRI = serotonin and noradrenaline reuptake inhibitor; TCA = tricyclic antidepressant.
* TRADE NAMES: amitriptyline – Endep; bupropion – Clorprax, Prexaton, Zyban SR; citalopram – Celapram, Celica, Ciazil, Cipramil, Citalobell, Talam, Talohexal; desvenlafaxine – Pristiq; doxepin – Deptran, Sinequan; duloxetine – Cymbalta; escitalopram – Esipram, Lexapro; mirtazapine – Avanza, Avanza SolTab, Axit, Mirtazon, Remeron; moclobemide – Amira, Aurorix, Clobemix, Maosig, Mohexal; nortriptyline – Allegron; reboxetine – Edronax; sertraline – Concorz, Eleva, Sertra, Setrona, Xydep, Zoloft; venlafaxine – Efexor-XR.

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Website resources for GPs and patients

Beyondblue

Downloadable fact sheets and resources for health professionals are available from: http://www.beyondblue.org.au/index.aspx?link_id=7.102

Downloadable information resources for patients are available from: http://www.beyondblue.org.au/index.aspx?link_id=7.980

- Resources relating to depression and chronic physical illness include fact sheets on coronary artery disease, after stroke, dementia, arthritis, asthma, Parkinson's disease, breast cancer and prostate cancer
- Resources relating to recovery from depression include fact sheets on reducing stress, sleeping well, keeping active, changing your thinking – cognitive behavioural therapy, reducing alcohol and other drugs (including smoking), other treatments for depression and anxiety, recovery, and healthy eating for people with depression, anxiety and related disorders

Resources mentioned in article

- **Anxiety disorders.** Fact sheet 21 and information card. Available at: http://www.beyondblue.org.au/index.aspx?link_id=7.980
- **Antidepressant medication. Advice for adults.** Fact sheet 11. Available at: http://www.beyondblue.org.au/index.aspx?link_id=7.980
- **SPHERE Questionnaire.** http://www.beyondblue.org.au/index.aspx?link_id=89.677

Black Dog Institute

Downloadable information sheets, fact sheets and other resources for health professionals and patients are available from: http://www.blackdoginstitute.org.au/healthprofessionals/resources/overview.cfm

Resources mentioned in article

- **About melancholic depression.** Depression information for GPs. Available at: http://www.blackdoginstitute.org.au/docs/3.AboutMelancholicDepression.pdf
- **An integrative depression model** and **Understanding your depressive episode.** An assessment and management tool, including a sheet for patients and doctors to work on together. Available at: http://www.blackdoginstitute.org.au/docs/UnderstandingYourDepressiveEpisode_000.pdf
- **A rational model for antidepressant drug prescription.** Available at: http://www.blackdoginstitute.org.au/docs/arationalmodelforantidepressantdrugprescription_000.pdf
- **Exercise and depression.** Fact sheet. Available at: http://www.blackdoginstitute.org.au/docs/ExerciseandDepression.pdf
- **Mindfulness in everyday life.** Patient handout. Available at: http://www.blackdoginstitute.org.au/docs/10.MindfulnessinEverydayLife.pdf
- **Quick relaxation techniques.** Patient handout. Available at: http://www.blackdoginstitute.org.au/docs/17.RelaxationSheetQuickRelaxationTechniques.pdf
- **Relapse signature: learning from experience.** Patient handout. Available at: http://www.blackdoginstitute.org.au/docs/18.RelapseSignatureLearningfromExperience.pdf
- **'Use it or lose it' – the benefits of exercise.** Patient handout. Available at: http://www.blackdoginstitute.org.au/docs/6.ExerciseUseitofLoseit.pdf

National Prescribing Service: Therapeutic Advice and Information Service

Drug information line for health professionals.

Telephone: 1300 138 677; online enquiry: http://www.nps.org.au/health_professionals/consult_a_drug_information_pharmacist/therapeutic_advice_and_information_service

often manifest as regrets, complaints, guilt and unresolved relationship difficulties. Dealing with 'unfinished business' is especially important in the context of a fatal disease.

Panic symptoms are common in patients with conditions such as asthma, chronic obstructive pulmonary disease, cardiac failure, severe pain and medical obesity. Some patients with these conditions may have a previous anxiety disorder that can worsen, with fears of possible death and disability due to their medical condition. Others may develop an anxiety problem as their medical condition worsens. Clinical psychologists can assist through cognitive behavioural therapy (CBT) techniques.

Appropriate use of exercise is extremely beneficial in its own right in most medical illnesses, even advanced heart failure. Aerobic exercise and weights training have antidepressant properties and also provide a feeling of empowerment and increase mobility and physical stability, as well as providing a greater sense of wellbeing, accomplishment and social support. Exercise can be prescribed; occupational therapists and physiotherapists can be helpful here. Information sheets on the prescribing of and benefits of exercise are available on the Black Dog Institute website (see the box on this page).

Stress management and relaxation techniques will assist with pain, sleep and apprehension and should improve relationships. Early techniques for stress management featured the 'power of positive thinking', and early relaxation techniques often involved progressive muscle relaxation with attention to breathing, such as Jacobsen's progressive relaxation, which was first described in the late 1930s. It is now recognised that there is a myriad of techniques to suit different personality types and coping styles. Some people encounter problems with 'letting go' and can become panicky when they try to relax. This needs to be discussed and a different type of relaxation technique

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considered. The trick is to match the type of relaxation exercises to the patient. An information sheet acting as a sampler of different techniques, so that patients can see what sort of exercise suits them, is available on the Black Dog Institute website (see page 6). Information sheets and material about anxiety and panic are also available on the beyondblue website (see page 6).

Physiotherapy can play an important part in the nonpharmacological treatment of depression. Many relaxation exercises emphasise breath control, which may be unhelpful when dyspnoea is part of the medical problem. Physiotherapists can assist with information about correct breathing posture, combined with appropriate relaxation strategies that do not focus on breathing.

CBT techniques can increase a patient's sense of mastery (promoting a sense of control), aid symptoms such as pain, insomnia and anxiety, and help prevent depression relapse.[2] Mindfulness is a form of self-awareness training adapted from mindfulness meditation. It has been described as a state of being in the present, accepting things for what they are. It was originally developed to assist with mood regulation in relation to pain and chronic illness and has been found to have considerable health benefits. An information sheet on mindfulness is available on the Black Dog Institute website (see page 6).

The experience of keeping a personal journal of their experience[10] and other creative techniques (such as art and poetry) can allow patients to express their emotions and help them make sense of the meaning to them of their illness.

Depression with medical comorbidity can challenge patients' coping styles. It is worth eliciting what works for them normally and during a crisis ('what's the biggest crisis you have had prior to your illness, and how did you deal with it?').

Many illnesses will raise issues of mortality and other spiritual and existential issues. It is important to ask whether the patient wants to talk about this and/or needs assistance from pastoral care or other spiritual/religious counsellors.

Pharmacological management

Feelings of depression and hopelessness can lead to the development of high blood pressure. Patients who feel depressed or hopeless have higher rates of cardiac arrhythmias and sudden cardiac death because of higher circulating levels of cortisol and noradrenaline, and also changes in heart rate variability and platelet aggregation. It is important to reassure and empower patients as much as possible and to treat depression prior to surgical interventions.

Dual action antidepressants – that is, the serotonin and noradrenaline reuptake inhibitors (SNRIs; desvenlafaxine [Pristiq], duloxetine [Cymbalta], venlafaxine [Efexor-XR]) – can improve depression, insomnia and pain tolerance simultaneously. For people with depression who are medically ill, compared with in otherwise well patients, it is even more important to start antidepressants at low doses and increase doses slowly because these patients are particularly prone to nausea, agitation and drug interactions. Information sheets about antidepressant drugs are available on the Black Dog Institute and beyondblue websites (see page 6). It is helpful to select target symptoms and consider the side effect profiles of medications. Medications should then be given for a trial period to address these goals, and stopped if they are not beneficial. It is wise to discuss the prescribing of antidepressants with the pharmacist and the patient's medical team. Advice about specific drug interactions can be sought from the National Prescribing Service's Therapeutic Advice and Information Service (see the box on page 6).

Pain, insomnia, multiple medications and interventions can all act to precipitate and prolong depression, and all are compounded where there is substance abuse involving prescribed and nonprescribed medications. It is important that treatment addresses all of these factors.

There is a complicated relation between substance use and mental illness, in that although people often start using substances in times of depression or stress, the substances themselves and the evolution of medical illnesses can lead to more mood disorders. Agents such as bupropion (Clorprax, Prexaton, Zyban SR) and nortriptyline (Allegron) are both antidepressant and anticraving, and other antidepressants can assist with mood maintenance after withdrawal. There are now several newer medications for use in drug dependence, such as varenicline (Champix) and buprenorphine (Subutex), and these make it possible for people to cease substance use relatively comfortably. The dosages of other medications need to be reviewed as plasma levels may change after smoking cessation; this can provide an incentive for smoking cessation.

Reappraisal further down the track

Some problems only become overt as time goes on. This can occur where there are developing illnesses, complications or emerging medical psychological issues. If the problems persist, it is important to take a fresh look and/or get a second opinion. Substance abuse issues also often only surface later.

On recovery from the depressive episode, it is important to 'have another look' at the patient to reassess any biological or personality vulnerability that can be improved to reduce the risk of relapse or recurrence. A resource for health professionals and an accompanying patient information sheet about understanding depression is available on the Black Dog Institute website (see page 6). This patient information sheet provides a framework for understanding what factors are important in the onset and course of depressive episodes for specific individuals. It is intended to be used collaboratively by individuals and their GPs

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to promote understanding of the depressive episodes and where treatment should be directed during the episode and what needs to be done to prevent recurrence.

There is also a patient handout about the concept of a ‘relapse signature’ on the Black Dog Institute website (see page 6). This resource provides information on learning from what happened in an episode of depression and how to ‘get in early’ and prepare for any further depressive episodes.

Conclusion

Depression in the context of medical illness is often viewed as being ‘understandable’ and not requiring treatment. The term ‘depression’ is used in a range of conditions, including normal experience (‘I’m depressed’…), personality traits (pessimism, self-criticism, worrying and tendency to ‘stress’) and adjustment reactions/disorders (including grief) as well as clinical disorders (major melancholic and nonmelancholic depressions). Differing approaches are required to treat the depression and enhance the patient’s ability to cope with the medical illness and other comorbidities. In those patients with multiple medical, psychiatric and substance use comorbidities, ceasing substance use can assist mental as well as physical health. MT

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COMPETING INTERESTS: Professor Wilhelm has written material for GP workshops on depression-related topics and also resources that appear on the Black Dog Institute website.

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MedicineToday 2009; 10(5): 32-44

Making sense of the complex depressed patient
Part 2: temperament and personality factors

Personality traits tend to be magnified in the presence of stress and depression – they 'shape' the presentation and add to the complexity of depressive episodes.

KAY WILHELM
AM, MB BS, MD, FRANZCP

Professor Wilhelm is Conjoint Professor, School of Psychiatry, University of NSW, and Senior Staff Specialist, Consultation–Liaison Psychiatry, St Vincent's Hospital, Sydney, NSW.

Depression may take many forms, and its manifestation in an individual is influenced by that person's temperament and personality style. Temperament is defined as an individual's characteristic behaviour and emotions as determined by his or her neurophysiological and emotional responses, which have biological and genetic underpinnings. Differences in some of the basic elements of behavioural functioning (such as autonomic reactivity, soothability, sleep–wake regularity and adaptability to change) are seen in babies and continue through life, but are also affected by the environment in which individuals are raised. These temperamental traits require epigenetic development and environmental exposure to become personality. Interestingly, 'personality' is derived from the Greek persona, meaning a mask, and Greek dramas used masks to typify

IN SUMMARY

- A person's temperament and personality style affects onset and course of illness, including depression, in that person.
- People with some personality styles are very vulnerable to episodes of major depression as well as chronic low mood.
- The combination of the patient's temperament and attachment style predict the best approaches to managing depressive episodes and the likely problems that may be encountered.
- Management of these depressions involves using a problem-based approach, identifying barriers, minimising harm and assessing the need and motivation for more long-term interventions.
- Antidepressants may be used to treat a depressive episode; assist with mood regulation, anxiety and aggression; and help patients cope with disintegration under stress.
- Case conferences, second opinions and supervision can all help to 'lessen the load'. A team approach can be useful but requires an integrated management plan.
- Different attachment styles invoke different emotional reactions from clinicians. GPs should consider the sorts of patients likely to 'push their buttons' and the best ways of responding.
- Patients should be reappraised after the depression has lifted as some personality dysfunction may resolve and enduring traits may need addressing to diminish vulnerability to further episodes.

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various characters rather than to disguise their identities.

Personality style has a pattern of pervasive effects on interactions with other people and function, and an impact on the abilities to relate, love and work. However, several personality traits cause people to be more prone to becoming depressed, staying depressed and having repeated episodes of depression. The inherent interpersonal problems lead to difficulties in dealing with the treating clinicians involved and treatment compliance.

The various methods of typifying personality styles vulnerable to depression differ in how they categorise people. However, they all aim to identify individuals with temperamental and personality factors that make them respond poorly to environmental stress, prone to misinterpreting ordinary situations as threatening, and have poorer emotional regulation and interpersonal skills.

This article aims to make sense of how personality style can be used to help manage patients with complex depression. This is necessary because:

- personality traits tend to be magnified in the presence of stress and depression – they 'shape' the presentation and add to the complexity of depressive episodes[1]
- temperamental and personality factors influence the type of treatment

Table 1. Personality styles*

Personality style	Characteristics	Coping styles	Schemas	CBT interventions
Anxious worrier	Highly strung, tense, nervy; worries about minor issues High scores on measures of neuroticism • When distressed: self-doubt, pessimism about future	Seeks out distracting activities, or seeks reassurance from others Makes long 'to-do' lists, engages in unproductive, time-consuming trivial activities	'The world is a dangerous place' 'I'm not being responsible if I don't worry about things' 'Worrying about things means that I care'	Anxiety management – relaxation training Mindfulness Problem-solving Graded exposure to frustration Goal setting Thought challenging
Irritable	Irritable or explosive when stressed Low frustration tolerance High scores on measures of neuroticism • When distressed: lashes out or criticises others, impatient with self	Indulges in reckless and/or pleasurable activities (e.g. gambling, alcohol use) that distract from underlying anxiety	'I'm useless unless I can control my temper' 'Good people do not express negative emotions' 'I must keep my worries and concerns to myself'	Anxiety management – relaxation training Anger management Graded exposure to frustration Communication skills
Self-critical	Pervasively low self-esteem Self-defeating and ineffective self-concept • When distressed: feelings of worthlessness, low sense of self-mastery and self-confidence	Relies on others to make decisions when distressed Blames self	'I'm not as good as everyone else' 'I'm incompetent' 'I need other people's reassurance'	Cognitive challenging Behavioural experiments Self-esteem building
Rejection sensitive	Highly sensitive to responses of others, reliance on reassurance from others Perceives rejection very easily • When distressed: feels empty, ruminates about feelings of abandonment	Engages in self-consoling behaviours, some of which may be isolating rather than problem-solving	'I'm unlovable' 'I'll be abandoned/left alone' 'I cannot survive on my own'	Assertiveness training Cognitive challenging Behavioural experiments

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- patients with some personality styles 'push the buttons' for their doctors more than do patients with other styles – these styles can be conceptualised in terms of the patient's attachment style.

Each personality style has characteristic difficulties with emotional regulation and problems with behaviour that can both 'kick-start' depressive episodes and also complicate and prolong episodes. This is bidirectional, as depression also tends to intensify the personality style. Cognitive therapy approaches can be used to improve these vulnerable styles but these interventions may not be possible while the patient is in the midst of a depressive episode. Once the period of distress and/or the depressive symptoms have abated, the personality traits should be reassessed.

The types and management of depression seen in people with a medical illness and the assessment and management of patients with melancholic depression are discussed in the other articles in this supplement.[2]

Typifying personality styles vulnerable to depression

The most common methods of typifying personality traits vulnerable to depression – vulnerable personality styles – are discussed below.

Table 1. Personality styles* continued

Personality style	Characteristics	Coping styles	Schemas	CBT interventions
Personal reserve	Avoids self-disclosure or honest reflection Tends to be formal, polite, reserved in social situations • When distressed: may withdraw from social interactions	Withdraws from others when distressed, does not easily disclose level of distress	'If people get to know the real me, they will know I am a loser' 'People cannot be trusted with personal information' 'I'm incapable of dealing with emotional issues'	Assertiveness and communication training Cognitive challenging Behavioural experiments Social skills training
Social avoidance	Tends to be shy and self-conscious Frequently avoids social interaction or hangs back socially • When distressed: withdraws from others	Withdraws from social interactions when distressed, engages in solitary activities	'I am a boring/ irritating/ unpleasant person to be with' 'I have nothing to say that would interest anyone' 'People look down on me'	Anxiety management – relaxation Cognitive challenging Behavioural experiments Activity scheduling Graded exposure
Perfectionist	Excessive attempts to control environment to reduce exposure to stress Very self-disciplined, conscientious, plans ahead • When distressed: ruminates over past behaviours and future decisions	Indulges in comfort foods, uses self-blame, displays behavioural paralysis Focuses on somatic symptoms/concerns	'I'm unworthy unless I am the very best' 'I'm a failure unless I can make everything work out well' 'Everything will fall apart if I don't control things'	Cognitive challenging Behavioural experiments Problem-solving and goal setting Relaxation Mindfulness
Self-focused	Unempathic – lack of consideration for others Sense of entitlement – tendency to blame others • When distressed: low frustration tolerance, anger and hostility towards others	Engages in risk-taking behaviours Blames others when distressed	'My needs need to be met by others' 'Other people cause me to get upset' 'The world owes me'	Anger management – and conflict resolution skills Appropriate assertiveness training Relaxation Mindfulness

* This personality style sheet is based on a body of work from the Black Dog Institute summarised in a book written by Professor Gordon Parker and Associate Professor Vijya Manicavasagar.[1] The sheet was produced by Professor Parker and Dr Sarah Weaver as part of a GP teaching program on CBT for patients with personality styles vulnerable to depression and is reproduced with their permission and that of the Black Dog Institute. More information is available in the book and on the Black Dog Institute website.

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Dimensional approaches

Dimensional approaches usually use self-reporting measures and structured interviews, including psychological and clinical assessments. These identify constructs that are thought to lead to vulnerable personality styles. One of the most widely recognised of these is neuroticism (the tendency to experience negative emotional states and high emotional reactivity). The Black Dog Institute (attached to the Prince of Wales Hospital in Sydney and affiliated with the University of New South Wales) has developed an integrated model of personality traits that lead to vulnerability to depression (Table 1).[1]

Diagnostic categories

Personality disorders can be categorised according to the diagnostic system commonly used by psychiatrists, mental health teams and clinical psychologists. One review of the influence of personality on major depression has noted higher rates of major depression in those people with personality disorders categorised according to the *Diagnostic and Statistical Manual of Mental Disorders*, 4th edition, text revision (*DSM-IV-TR*; Table 2).[3,4] The *DSM-IV* system may assist GPs in classifying their patients but is not especially helpful as a framework for developing effective management strategies. People with personality disorders can have significant problems with social functioning as well as being more vulnerable to more complex and less typical depression, often in the context of other psychiatric comorbidities.[5] The *International Classification of Diseases*, 10th edition (*ICD-10*) is not as widely used as the *DSM-IV* system but is included for comparison (Table 2).[6]

Patients' attachment styles

There has been increasing interest recently in the identification of the attachment styles of patients, with an appreciation of their impact on the doctor–patient relationship and treatment outcomes (Table 3).

Using the attachment model, personality disorders arise through infants developing neurophysiological processes to achieve homeostasis after emotional arousal.[7] This happens because of their genes and environment, and particularly their exposure to attachment figures who provide an 'emotional template' so that the infant grows up with difficulties in emotional regulation and ability to relate to others.

Viewing patients with personality dysfunction in these terms can provide greater understanding of their depression and treatment needs.

Complex depression and personality style

Assessing personality style in depressed patients is fraught with difficulties and requires a longitudinal perspective. Points to be considered include:

- a longstanding behaviour pattern indicates personality style in patients; however, people with vulnerable personality styles are more likely to become depressed than others
- it is important (but not always possible) to disentangle the effects of substance use
- a recent change in behaviour may indicate depression, medical illness and/or early cognitive decline, which all need to be excluded before a personality disorder can be diagnosed
- the characteristic depression associated with a personality disorder is a longstanding dysphoria, associated with poor self-esteem and tendency to emotional dysregulation, and is usually nonmelancholic in nature
- of note, patients who have agitated melancholic depression present with needy, clingy behaviour evoking irritation that may be mistaken as part of a personality disorder; however, the behaviour abates with resolution of the depressive episode.

Complex depression and attachment style

Attachment style is a useful way of conceptualising problems associated with engaging the patient and understanding the interpersonal dynamics of the clinical interaction. The various attachment styles each have different pitfalls that can impact on motivation and the treatment alliance. The insecure attachment styles are all related to onset and prolongation

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of clinical depression,[8] and it is often these factors that render depressive episodes more complex in the context of vulnerable personality styles. Table 3 summarises some of the pitfalls for clinicians associated with the different styles, which are all likely to be magnified when the patient is depressed.

Secure attachment style

Patients with a secure attachment style comprise about half of the general population. Such people demonstrate the ability to trust in their own emotions and insights and have a productive, relatively straightforward interaction with their clinicians. They have good self-esteem and a supportive social network. They will still be (appropriately) anxious and fearful when dealing with stressful situations but will have less additional 'emotional baggage'. They may still become depressed, particularly in the context of some of the medical problems noted in the previous article on complex depression.[2]

Anxious/preoccupied attachment style

Patients with an anxious/preoccupied attachment style demonstrate compulsive help-seeking, in the context of anxiety and fear, low self-esteem and lack of belief in their ability to cope. They find it difficult to accept reassurance and to trust caregivers. Therefore, they may repeatedly see their GP with a symptom, being unable to accept the GP's reassurance that the symptom is not a sign of serious disease.

These patients do better with clinicians who are constant, reliable and not unduly anxious themselves.[9,10] It has been recommended that these patients are given regular brief appointments that are not contingent on symptoms. They are encouraged to become more self-reliant (make lists of questions, make own enquiries). If they require antidepressants, they will benefit most from those that are more sedative, such as mirtazapine (Avanza, Axit, Mirtazon, Remeron). In complex cases, there is the possibility of dependence on sedatives/hypnotics and/or alcohol as known or unknown complications.

The anxious/preoccupied attachment style has similarities with the anxious and internalising personality styles in Table 1 (that is, the anxious worrier, self-critical, rejection sensitive, personal reserve and social avoidance styles). Psychological treatment for patients with these styles is likely to aim to increase patients' control over anxiety and fear, and emotional regulation in general, and to improve their self-esteem. Some suggested cognitive behavioural therapy (CBT) approaches are given in Table 1.

Avoidant/fearful attachment style

Patients with an avoidant/fearful attachment style demonstrate approach/avoidance behaviour. They are aware of their needs for interpersonal relationships but are wary of getting involved, so they leave problems until the last minute and then want immediate attention. Compared with people of other attachment styles, they have lower levels of health care utilisation. They often make last minute appointment changes or cancellations and they are likely to present with somatic complaints rather than identify depression, anxiety or other mental health issues.[10]

With avoidant attachment, it is helpful to identify clear, transparent goals that patients can relate to, while validating their concerns. These patients are wary of placing trust in individuals and may do better relating to a team approach, at least until a therapist providing long-term continuity is available. In complex cases, there is often a web of unfinished and unsatisfactory previous clinical interactions that can cause confusion for both patient and doctor.[10]

Psychological treatment for those patients with anxiety and ambivalence over relationships aims to increase control over anxiety and fear, and emotional regulation in general, and to improve self-esteem. Again, suggested CBT approaches are given in Table 1.

Table 2. A summary of the *DSM-IV-TR* and *ICD-10* personality type clusters[4,6]

Cluster A (odd or eccentric disorders)

- Paranoid – longstanding suspiciousness; generalised mistrust of others
- Schizotypal – social isolation, odd behaviour and thinking
- Schizoid – lack of interest in social relationships, tendency to a solitary lifestyle, secretiveness, emotional coldness

Cluster B (dramatic, emotional or erratic disorders)

- Antisocial – disregard for/violation of rights of others, deceit, manipulation; called 'dissocial' in *ICD-10*
- Borderline/histrionic – instability in mood, chaotic/unstable interpersonal relationships, self-image, identity and behaviour; called 'emotionally unstable' in *ICD-10*
- Histrionic – pervasive attention-seeking behaviour, including inappropriate sexual seductiveness and shallow or exaggerated emotions
- Narcissistic – grandiose sense of self-importance, belief they are 'special', unique, sense of entitlement, lack of empathy

Cluster C (anxious or fearful disorders)

- Avoidant – social inhibition, inadequacy, extreme sensitivity to negative evaluation, avoidance of social interaction; called 'anxious avoidant' in *ICD-10*
- Dependent – pervasive psychological dependence on other people
- Obsessional – general psychological inflexibility, rigid conformity to rules and procedures, perfectionism, moral code and/or excessive orderliness; called 'anankastic' in *ICD-10*

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continued

Table 3. Relation between attachment style, vulnerable personality traits and *DSM-IV* personality dimensions*

Patient's attachment style	Impact on interaction with doctor	Doctor's reaction to specific style	Depression prone personality styles[†]	Difficulties with affect regulation	*DSM-IV* equivalent cluster	Pitfalls for clinician	Patient outcomes
Secure	Clear history Collaborative, trusting approach	Feels empathy, appreciated, sympathetic to patient's needs	Presence of traits that do not lead to social disability or depression	Able to soothe self and use internal/ external resources, flexible strategies; appropriate use of anger, humour	Presence of traits rather than disorder	Doctor may treat the patient as a friend	Any loss of objectivity leads to personal and health issues being overlooked
Anxious/ preoccupied	Uses support appropriately Anxious, co-operates after reassured Lengthy, overinclusive, vague history Compulsive help seeking	Feels need to reassure patient initially, but later may feel irritated, overwhelmed	Anxious worrier Self-critical Rejection sensitive	Under-regulation of social emotions, e.g. shame and guilt, also anxiety and sadness Positive affects experienced in the company of others	Cluster C Anxious/ fearful	Patient expects doctor to make decisions 'I can't…' 'You know best'	Resistance (yes, but…); anxiety, regressed, may leave
Avoidant/ fearful	Wary, doesn't trust doctor, misses appointments Less likely to seek treatment	Frustrated at lack of involvement, unreliability, feeling of incompetence, intrusion, wish to withdraw	Personal reserve Social avoidance Perfectionist	Under-regulation of fear, over-regulation of positive emotion, leading to narrow emotional range	Cluster A Odd/ eccentric	Doctor may become frustrated and bully patient, who says 'I can't…' 'I forgot…' 'I really couldn't say…' 'You know…'	Increased anxiety, depression, threats of self-harm, often angry withdrawal
Dismissive/ demanding/ disorganised	Gives little personal detail Treatment not thought helpful Compulsive self-reliance	Feels 'put down', patronised, angry, rejected Relief when patient fails to attend	Irritable Self-focused	Problems regulating all positive/negative affects, mainly seen in regulation of fear, anger, sadness, anxiety	Cluster B Dramatic/ emotional/ erratic	Doctor may get angry and confront patient, who says: 'You can't help me anyway…' 'You're the doctor, you should know'	Anger/ resistance, complaints, threats

* This material is intended to give a rough outline of how the different systems fit together; it is not exhaustive and is intended as a guide only.
† See Table 1.

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Table 4. Assessing and managing depression in patients with personality disorders

Patient feature	Assessment/intervention
Is there a significant change in mood? What is the patient's normal mood state?	People with some personality traits are more vulnerable to superimposed episodes of major depression that require symptomatic treatment but when resolved may still leave the patient with their more chronic depression
What type of depression?	Check there are no features suggesting a melancholic and/or psychotic depression. Treat accordingly if these features are present; may be best to start with SNRIs. Information sheets about antidepressant use are available on the Black Dog Institute ('A rational model for antidepressant drug prescription') and beyondblue ('Antidepressant medication. Advice for adults. Fact sheet 11') websites* After those depressions have been excluded, consider psychological approaches for short-term symptom relief For antidepressants, low doses of SSRIs are generally the best starting point – start at half-tablet of selected SSRI unless there is evidence of medication sensitivity suggesting patient is a slower metaboliser, in which case use quarter-tablet. Increase dosage slowly (if required) to prevent emergence of side effects and improve compliance. SNRIs are useful for incomplete response or if effective previously
What type of anxiety?	Ask whether anxiety was a problem in childhood – this is an important feature in both some personality styles and vulnerability to repeated depressive episodes. Panic can be a common concomitant of styles linked to anxiety, rumination and emotional dysregulation. Dealing with panic gives a greater sense of self-control
Is there a history of regular use of nicotine, alcohol, cannabis, sedatives, stimulants or other substances?	Assess history and degree of reliance on these substances – all may affect onset and perpetuation of depression and compound personality dysfunction
Is there mood dysregulation?	Psychological approaches include problem-solving, relaxation, mindfulness and prescribing exercise. Information sheets on these are available on the Black Dog Institute website* A mood chart ('Daily mood chart and monitoring your progress', available on the Black Dog Institute website) can track progress and continue to check for substance use, gambling and other self-destructive behaviours*
Is there a history of mood swings or emotional instability?	It can be difficult to disentangle early bipolar disorder from adolescent turmoil and evolving borderline personality features, particularly in the presence of substance abuse. A mood chart ('Daily mood chart and monitoring your progress', available on the Black Dog Institute website) may assist* Check for presence of bipolar disorder – the self-report test 'Bipolar disorder self-test' (available on the Black Dog Institute website) may help*

Dismissive attachment style

Patients with a dismissive attachment style demonstrate compulsive self-reliance. They lack trust in others because of past rejections. Their relationships can reflect a lack of trust that 'anything can be done'. As with patients with the avoidant/fearful attachment style, these patients are wary of placing trust in individuals and may do better relating to a team or clinic approach, at least until a therapist providing long-term continuity is available.

It is recommended that these patients be allowed to determine the interpersonal distance and that their clinicians do not become too familiar with them and allow them some flexibility. For example, these patients appreciate some limited choice in their treatment options. They may do better having some communication through phone calls, using proactive reminders. In complex cases, there is also a high possibility of poor compliance with treatment and reluctance to engage with others as likely complications. They may also 'self-medicate'.

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Table 4. Assessing and managing depression in patients with personality disorders continued

Patient feature	Assessment/intervention
What type of attachment style is exhibited?	See Table 3
Are there current stressors precipitating depression or impeding recovery?	Offer short-term strategies such as stress management skills, relaxation skills, problem-solving, counselling, family support to 'clear the way' through current problems and allow a reappraisal of personality factors once crisis has resolved
Are there long-term interpersonal difficulties?	Identify problems, offer interpersonal or relationship therapy; longer term psychotherapy may be required (see 'Longer-term strategies' on page 43)
Are there unresolved issues related to loss, anger, guilt, self-blame, bereavement or previous trauma?	Such 'unfinished business' often underlies complex depression Clarify misunderstandings, guilt issues, acknowledge 'unfinished psychological business'
Are there ongoing undue concerns with health? Is there somatising behaviour? Is there a long history of health anxiety or is it recent?	Use reattribution techniques to illustrate relation between psychological issues and body function [8] Check whether somatising behaviour indicates past trauma, including physical and sexual abuse; these problems may require psychotherapy[5]
Is this part of a borderline picture?	For people with borderline traits, a management plan can provide better co-ordination of services; best to have a therapist who understands principles of treating personality disorders
Is there worrying, ruminations, obsessional thinking or rituals? Are these part of the personality style, made worse when patient is stressed/depressed, or only part of a depressive episode?	Consider using an SSRI (sertraline and escitalopram have the least interactions with other medications and are the best tolerated) or an SNRI (desvenlafaxine, duloxetine or venlafaxine); start low, increase slowly to avoid side effects. Other SSRIs include citalopram, fluoxetine, fluvoxamine and paroxetine[†] Patients with a 'worrying' temperament may require longer term use of SSRIs and/or psychological intervention
Is there a risk of DSH)? Have there been previous DSH attempts (including wrist cutting)?	The history of frequent attempts, often with wrist cutting and early eating disorders is more a feature of the Cluster B style of personality disorder, where there are significant mood swings and fears of abandonment DSH is more likely in the setting of interpersonal crises and disinhibition from substance use; DSH risk should be considered when choosing an antidepressant

ABBREVIATIONS: DSH = deliberate self-harm; SSRI = selective serotonin reuptake inhibitor; SNRI = serotonin and noradrenaline reuptake inhibitor.

* Websites: Black Dog Institute – http://www.blackdoginstitute.org.au; beyondblue – http://www.beyondblue.org.au

† TRADE NAMES: SSRIs: citalopram – Celapram, Celica, Ciazil, Cipramil, Citalobell, Talam, Talohexal; escitalopram – Esipram, Lexapro; fluoxetine – Auscap 20 mg Capsules, Fluohexal, Fluoxebell, Lovan, Prozac, Zactin; fluvoxamine – Faverin, Luvox, Movox, Voxam; paroxetine – Aropax, Extine, Paxtine; sertraline – Concorz, Eleva, Sertra, Setrona, Xydep, Zoloft. SNRIs: desvenlafaxine – Pristiq; duloxetine – Cymbalta; venlafaxine – Efexor-XR.

Psychological treatment needs to address the deep sense of mistrust, lack of confidence in others and poor self-esteem of people with this attachment style. It is likely to aim to increase control over impulsivity and anger, and emotional regulation in general.

This attachment style has some similarities with, but does not overlap, the more externalising personality styles (the irritable and self-focused styles). Some suggested CBT approaches are given in Table 1.

Disorganised attachment style

The disorganised attachment style is a less common style than the others mentioned and arises in people who have extremely aberrant relationships, often resulting from an abusive childhood. These patients tend to disintegrate under stress and may develop transient psychotic symptoms. They respond to a consistent, predictable approach with clear limits and goals. Short-term antipsychotics (low doses of typical antipsychotics such as chlorpromazine [Largactil; 10 to 50 mg] or

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second-generation antipsychotics such as risperidone [Rispa, Risperdal, Rixadone; 0.5 to 2.0 mg]) can be useful in these patients. Psychological techniques to increase mood regulation (for example, exercise and mindfulness) can also help.

This style overlaps with the more extreme cases of the externalising irritable and self-focused personality styles. In complex cases, the possibility of substance abuse is likely to perpetuate depression and profound and transient mood swings.

Management

A guide to assessment and management of depression in people with personality disorders is provided in Table 4. The Black Dog Institute website has a self-rated personality questionnaire that identifies vulnerable personality styles – the 'Temperament and personality questionnaire' (see the box on this page). The 'Integrative depression model' sheet on the same website can be used to discuss how the biological and psychosocial factors fit together. This can then lead to a discussion of the motivation the patient has to change.

Management is directed by the insight patients have into their personality style and the motivation they have to change. People with personality disorders often report longstanding depression ('I've been depressed for as long as I can remember'), and this requires a more psychologically based approach. There is no specific pharmacological treatment but antidepressants can relieve superimposed depressive episodes and may provide symptomatic relief in some cases. Information sheets about antidepressant drugs are available on the Black Dog Institute and beyondblue websites (see the box on this page).

Immediate symptomatic relief and short-term strategies

Immediate relief of symptoms and short-term management of depression in people with personality disorders can be provided by the following strategies:

- using the 4 'D's (delay, deep breathing,

Website resources for GPs and patients

Beyondblue

Downloadable fact sheets and resources for health professionals are available from: http://www.beyondblue.org.au/index.aspx?link_id=7.102

Downloadable information resources for patients are available from: http://www.beyondblue.org.au/index.aspx?link_id=7.980

Resources mentioned in article

- **Antidepressant medication. Advice for adults.** Fact sheet 11. http://www.beyondblue.org.au/index.aspx?link_id=7.980
- **Lifestyle factors** – resources relating to lifestyle factors, including those listed below, are available at: http://www.beyondblue.org.au/index.aspx?link_id=7.980
  - **Reducing stress.** Fact sheet 6.
  - **Keeping active.** Fact sheet 8.
  - **Reducing alcohol and other drugs (including smoking).** Fact sheet 9.
  - **Healthy eating for people with depression, anxiety and related disorders.** Fact sheet 30.

Black Dog Institute

Downloadable information sheets, fact sheets and other resources for health professionals and patients are available from: http://www.blackdoginstitute.org.au/healthprofessionals/resources/overview.cfm

The psychological toolkit – a collection of practical resources for GPs to assist in the management of mood disorders. Materials include fact sheets for GPs and patients (including on problem-solving, relaxation, mindfulness and exercise), questionnaires for assessment of depression, charts of treatment protocols and tools for self-monitoring. http://www.blackdoginstitute.org.au/healthprofessionals/resources/thepsychologicaltoolkit.cfm

Resources mentioned in article

- **An integrative depression model.** Can be used to discuss how the biological, psychosocial and personality factors fit together – http://www.blackdoginstitute.org.au/docs/1.IntegrativeDepressionModel.pdf
- **A rational model for antidepressant drug prescription.** http://www.blackdoginstitute.org.au/docs/arationalmodelforantidepressantdrugprescription_000.pdf
- **Bipolar disorder self-assessment test.** The clinician version has background and scoring as well as the assessment test – http://www.blackdoginstitute.org.au/docs/selfassessmentofbipolardisorderclinicianversion_000.pdf. The patient version, the 'Bipolar disorder self-test', can be completed online, with scoring – http://www.blackdoginstitute.org.au/public/bipolardisorder/howtotell/self-testing.cfm
- **Daily mood chart and monitoring your progress.** Patient sheet for people with depression – http://www.blackdoginstitute.org.au/docs/11.MoodChartforDepressionandhowtomonitoryourprogress.pdf
- **Exercise** – fact sheets and handouts on the benefits of exercise for people with depression, exercise recommendations and plan development are provided in the 'Psychological toolkit' mentioned above
- **Omega-3 and mood disorders.** Background information and recommended intake levels – http://www.blackdoginstitute.org.au/docs/Omega-3andmooddisorders.pdf
- **Temperament and personality questionnaire.** An assessment tool for completion by patients – http://www.blackdoginstitute.org.au/healthprofessionals/resources/assessmenttools.cfm#TPQ

Education programs for GPs

The Black Dog Institute provides specialised education and training programs on the identification, treatment and management of depression and bipolar disorder for GPs and GP registrars in NSW. These are available to a limited extent to GPs in other States and Territories. Further information is available from: tp://www.blackdoginstitute.org.au/healthprofessionals/educationtraining/gps/index.cfm

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drink water and distraction), which can provide a circuit breaker to assist emotional 'de-arousal', followed by the use of relaxation or mindfulness techniques to ease depression relapse, anxiety and irritability
- participation in exercise, which will improve emotional regulation; many patients find walking, using weights and swimming useful (information sheets about exercise and depression are available on the Black Dog Institute website) – this can be followed by discussion of strategies to create a healthier lifestyle
- reassurance that people mellow as they grow older and that the affective instability related to some vulnerable personality styles tends to improve with age
- harm minimisation regarding risk taking, 'acting out' behaviour and substance abuse, using education and counselling
- using problem-solving strategies to deal with immediate crises and anticipate future ones (has been proven useful in patients with personality disorders)[11]
- using antidepressants to alleviate depression and anxiety symptoms; choice is guided by side effect profile and consideration of the possibility of overdose or interaction with alcohol, nicotine and other substances
- using a selective serotonin reuptake inhibitor (SSRI) or a serotonin and noradrenaline reuptake inhibitor (SNRI) to assist with affect regulation, ruminations and compulsive behaviours, as well as depression; these are relatively safe in overdose, and sertraline and escitalopram have been identified as having the most acceptable side effect profile,[12] as well as low interactions with other medications (see Table 4 for full list of SSRIs and SNRIs)
- antidepressants can also provide mood stability in the context of mood dysregulation.

Medium-term strategies

Medium-term strategies for people with personality disorders and depression include:

- addressing lifestyle factors, such as healthy eating, exercise, stopping smoking and substance use, controlled drinking and dealing with stress, indirectly assists depression (and improves vascular risk factors) even in the absence of psychological insight; information sheets to assist with these are available on the Black Dog Institute and beyondblue websites
- addressing any substance use; nicotine dependence and alcohol and substance abuse have been linked with chronic depression and increased suicidal ideation[2]
- using psychological strategies for mood regulation and cognitive techniques for vulnerable personality types,[1] such as the CBT strategies outlined in Table 1
- using omega-3 fatty acids, which have been shown to be useful in improving emotional regulation for those with continued suicidal ideation and borderline traits; an information sheet on the use of omega-3 fatty acids in depression is available on the Black Dog Institute website
- continuing use of antidepressants may be useful in the medium term if they have proved effective at relieving chronic depression or ongoing suicidal ideation or improving mood dysregulation (e.g. anxiety, obsessional ruminations, irritability).

Longer-term strategies

There is good evidence for the effectiveness of psychodynamic therapy, CBT and dialectical behaviour therapy for people with personality disorders.[13] Dialectical behaviour therapy is a CBT approach for treating people with borderline personality disorders. It covers four main treatment areas: learning mindfulness skills, increasing interpersonal effectiveness with assertiveness and problem-solving, improving emotional regulation, and improving distress tolerance.

These approaches require skill and experience and are not always readily available. It is expected that a trained psychiatrist and/or clinical psychologist will generally undertake these treatments in more complex cases. Patients may attend specialist programs and day services, depending on access and motivation.

The severe end of the personality disorder spectrum

At the severe end of the spectrum, personality disorders are likely to have serious consequences. 'Red flags' for GPs regarding serious personality disorders include:

- multiple attempts at deliberate self-harm
- severe substance abuse
- history of assaults, antisocial behaviour and lack of remorse
- pattern of continuing dysfunctional relationships
- pattern of visiting multiple doctors, none of whom are 'good enough'
- pattern of being overly familiar or interpersonally involved with treating clinicians
- sporadic or dysfunctional work record
- pattern of interpersonal problems.

An important issue is that once the presence of a personality disorder is established it is sometimes forgotten when other mental illness, particularly a severe condition such as a melancholic depression or bipolar disorder, present. However, the converse is also true: 'When the personality characteristics are prominent, there is a tendency for hard-pressed clinical staff to want to exclude such patients from inpatient care as they appear to be less deserving than other patients. This may be a mistake unless special attention is paid to treating the personality disorder as well as the mental illness'.[11]

It is often puzzling to GPs why some people with complex personality disorders (particularly Cluster B – the dramatic, emotional or erratic disorders) are not

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admitted to hospital routinely when they are distressed, depressed and suicidal. This is usually because these people have had several previous admissions that either have not made a difference or have caused them to become more distressed or disorganised. This situation makes more sense when attachment styles are considered. It is important for GPs and mental health teams to work together with a shared management plan to avoid misunderstandings between clinicians and mixed messages to the patient.

Reappraisal down the track

It is essential to re-evaluate a patient's personality style once the depressive episode has resolved because in some people the personality dysfunction resolves along with the depressive episode. This is particularly the case for patients with agitated melancholic depression, but can occur in those who are very distressed by marked emotional dysregulation.

For other patients with resolved depressive episodes, enduring personality vulnerabilities become apparent. Patients are then in a better condition to appraise the need for further assistance to diminish vulnerability to further episodes.

Conclusion

A person's temperament and personality style affects the onset and course of illness, including depression, in that person. Several personality traits cause people to be more prone to becoming depressed, staying depressed and having repeated episodes of depression. The inherent interpersonal problems lead to difficulties in dealing with the clinicians involved and treatment compliance.

In the short term, GPs can use psychological approaches (relaxation, mindfulness, exercise) to promote problem-solving skills and greater emotional regulation along with harm minimisation strategies in patients with personality disorders and depression. More intense psychotherapy is appropriate in patients who are motivated, and pharmacological treatment can alleviate depression and anxiety symptoms and assist with mood regulation. It is important to reappraise patients after the depression has been lifted as some personality dysfunctions may resolve and enduring traits may need to be addressed to diminish vulnerability to further episodes.

Case conferences, second opinions and supervision can all help to 'lessen the load'. A team approach can be useful but requires a management plan so that roles for various clinicians are clear to both the team and the patient. MT

Acknowledgements

The author would like to thank Dr Sarah Weaver for comments on this article, and Professor Gordon Parker for access to Black Dog Institute material.

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COMPETING INTERESTS: Professor Wilhelm has written material for GP workshops on depression-related topics and also resources that appear on the Black Dog Institute website.

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MedicineToday 2009; 10(6): 22-34

Making sense of the complex depressed patient
Part 3: melancholic and psychotic depression

Melancholic depression can occur in patients of any age but is more likely to have first onset in patients aged over 60 years. Patients with earlier onset melancholic depression are more at risk of developing bipolar disorder.

KAY WILHELM
AM, MB BS, MD, FRANZCP

Professor Wilhelm is Conjoint Professor, School of Psychiatry, University of NSW, and Senior Staff Specialist, Consultation-Liaison Psychiatry, St Vincent's Hospital, Sydney, NSW.

Many factors may complicate the presentation and course of depression in an individual. Contemporary thinking is that biological or psychosocial factors either alone or in combination can 'kick start' a depressive episode and that episodes may be melancholic in type in patients with the prerequisite genetic and other biological vulnerabilities. This is an advance on the categorisation of depression using the terms 'reactive' and 'endogenous' depression, where 'reactive' depression implied that the episode would resolve when the triggering event was resolved and 'endogenous' implied the episode arose solely from some physical process and only 'biological' interventions could assist.

IN SUMMARY

- **Melancholic depression and psychotic depression (melancholic depression with associated psychotic features) are associated with significant morbidity and high suicide risk.**
- **Melancholic depression is more commonly late onset (patients over the age of 60 years) and related to microvascular disease or other neurodegenerative and illness-related factors – structural melancholia.**
- **Early-onset melancholic depression (often before the age of 30 years) has a genetic predisposition – functional melancholia. These patients have an increased risk of developing bipolar disorder.**
- **Diagnosis relies on symptoms (anhedonia, non-reactivity, diurnal mood variation and early morning wakening) and observable features of psychomotor disturbance involving retardation and/or agitation with impaired cognitive processing (poor concentration and inattention).**
- **Red flags for melancholic depression include sudden and significant change in behaviour, poor sleep, sudden unexplained appetite loss, sudden inability to work effectively and complaints about being unable to think, unusual ruminations and/or preoccupations, and talk of hopelessness.**
- **Dual-action antidepressants are the treatment of choice for melancholic depression; the serotonin and noradrenaline reuptake inhibitors (SNRIs) are first line, followed by tricyclic antidepressants. Psychotic depression is treated with antidepressants and antipsychotics.**

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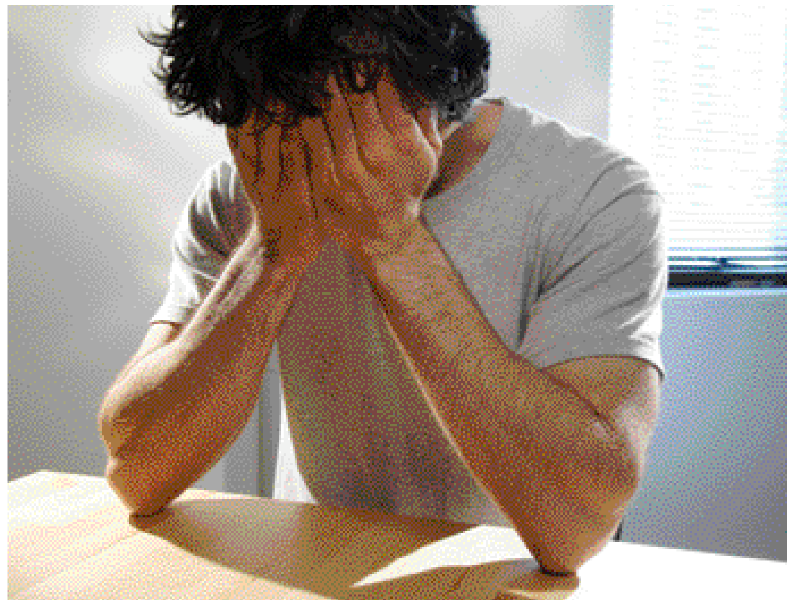
Earlier onset depressions are more likely to be associated with a strong family history, perhaps because of an inherited vulnerability to stress-related depression and anxiety, or neuroticism. These depressions are much more likely to be nonmelancholic in nature but there is a small but significant group of people who have early-onset melancholic depression. These patients have an increased risk of developing bipolar disorder. Late-onset depressions are more likely to be melancholic and/or psychotic and are related to microvascular disease or other neurodegenerative and illness-related factors, with different treatment implications and outcomes. Melancholic depression usually requires treatment with an antidepressant, and is associated with significant morbidity and high suicide risk.

This article discusses the assessment and management of patients with melancholic depression. Bipolar disorder is not discussed in detail in this article but is the subject of articles in the August to November 2009 issues of *Medicine Today*. The presentations and management of depression in people with a medical illness and how personality style can be used to help manage patients with complex depression are discussed in the other articles in this supplement.[1,2]



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Melancholia and depression

'Melancholia' is a term that was used in the 2nd century AD by Soranus of Ephesus, a Greek physician practising in Rome, to describe individuals exhibiting 'mental anguish and distress, dejection, silence, animosity towards members of their household, sometimes a desire to live, and at other times

Table 1. Functional and structural melancholic depression[4]

Functional melancholia	Structural melancholia
Generally early onset, often before the age of 30 years	Associated with later onset (patients aged over 60 years)
Associated with genetic predisposition such as a family history of depression or bipolar disorder, or change in neurotransmitters after use of some medications (e.g. corticosteroids) or illicit drugs (e.g. cocaine or amphetamines) in vulnerable people	Usually associated with vascular predisposition
Structural abnormalities rare on imaging	Structural abnormalities commonly seen on neuroimaging – usually white matter hyperintensities secondary to microvascular infarcts
Hypothesised mechanism is functional shut-down of circuits linking the basal ganglia and prefrontal cortex	Hypothesised mechanism is structural disruption of circuits linking the basal ganglia and prefrontal cortex; about one-third of patients develop dementia within five years
Has more pronounced inanition, fatigue and lack of motivation than late-onset melancholia, as well as cognitive difficulties	Has more pronounced psychomotor slowing, often with agitation, than early-onset melancholia; as well as inanition, lack of motivation and cognitive difficulties
Good response to broad spectrum antidepressants or electroconvulsive therapy (ECT)	Poorer response to antidepressants and ECT, perhaps with risk of delirium

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Table 2. Assessing patients with melancholic depression

Assessment issue	Questions to ask patient
Does the patient have a depressive episode?	• Are you depressed? • Has there been a change in self-esteem and/or self-worth? • Are you being more self-critical or tough on yourself than usual? These are followed by questions related to depression – appetite loss, sleep loss, loss of interest and motivation, loss of concentration, guilt, suicidal ideation and plans
Does the patient have a melancholic depression?	• How are you spending your day? How different is this from normal? • Are you able to look forward to things you normally enjoy? • Can you be cheered up? Do you enjoy activities as much as usual when you get started? What lifts your mood? • How are you sleeping? What time are you waking up? What is your normal time? • Is there a change in your mood and energy over the day? Has this a specific pattern? • Have you found it difficult to get going, especially in the mornings? Have you had difficulty getting out of bed and/or showering? Have you felt apathetic? • Have you felt empty inside? • Are you preoccupied with any thoughts or ideas? Have you any worries that seem to be getting you down? Are you worrying about things you wouldn't normally worry about?
Have there been any manic episodes? Is there a personal or family history of bipolar disorder?	• Have you ever had any mood swings where you are more energetic or 'wired'? • Has anyone ever said you were manic?
Is there evidence of psychotic depression?	• Some people find that when they are stressed, they have unusual experiences such as being overly concerned about money or health, or regrets that normally wouldn't be of concern. Have you had any such experiences? • Have you been a lot more worried about… than usual? • Have you had any unusual thoughts? • Have you thought that your illness is a punishment? • Have you felt that your life was in danger?
What is the age of first onset?	• Have you had episodes like this before? • How old were you the first time you had an episode?
Does the patient have any medical problems?	• Have you a new medical problem? What do you think is causing this? • Are you taking any new medications?
Are there any risk issues related to severity?	• Have you thought that life was hopeless/not worth living/you would be better off dead? Have you any plans to hurt yourself? • Have you been waking earlier than usual? What time? • What is on your mind when you awake?

a longing for death; suspicion that a plot is being hatched against him, weeping without reason, meaningless muttering, and occasional joviality'.[3] This description is still clearly recognisable today, and the term has endured.

Melancholia is best conceptualised as a severe mood disorder superimposed on a fronto-subcortical network disruption disorder that causes psychomotor disturbance characterised by problems with cognitive functioning (problem solving, planning, social interaction) and slowing of mental and motor activity, often with associated periods of agitation. The disruption may be functional, as is generally seen in early-onset depressive disorders, or structural, as is generally seen in late-onset presentations (Table 1).[4]

The assessment of melancholia needs to consider the age of onset, presence of medical problems, bipolar disorder or psychosis, and risk issues related to severity and suicidal thoughts.

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The early onset of melancholic depression, with or without psychotic features, prompts the possibility of drug-induced depressive episodes, an underlying medical problem affecting the central nervous system or an evolving bipolar disorder or other psychotic illness, even in the absence of periods of elation, which may arise later. These possibilities should be explored.

The underlying pathological process in the structural melancholia group is commonly related to cerebrovascular disease. The term 'vascular depression' has been coined to describe depression developing in patients aged 60 years or older who have a high number of vascular risk factors such as hypertension or smoking.[7] It has been noted that patients presenting with vascular depression typically show greater cognitive dysfunction, functional disability, psychomotor retardation and anhedonia, and less agitation, guilt and psychosis than those with nonvascular depression.[8]

Repeated episodes of melancholic depression have been associated with decreased brain volume in the basal ganglia and hippocampus.[5] One study reported that decrease in brain volume is related to the duration of depression prior to the taking of antidepressant medication and it appears that antidepressants may have a neuroprotective role.[6]

Patients with melancholic depression of either early or later onset are at risk of further depressive episodes, which are generally severe and do not resolve spontaneously. It is worth keeping a 'watching brief' on all these patients.

In patients with psychotic depression (melancholic depression with associated psychotic features such as loss of insight, delusions and hallucinations, guilty ruminations), delusions are more common than hallucinations. The delusions (such as 'I'm a failure', 'I have no money', 'I have sinned', 'I have cancer') are generally consistent with mood, less bizarre and may seem appropriate as exaggerations of some current situation. However, these patients remain inconsolable even after reasonable and frequent reassurance to the contrary. The presence of agitation and other profound psychomotor change in psychotic depression is very distressing for the patient and can lead to serious harm to self and/or others. These features should be treated as a psychiatric emergency.

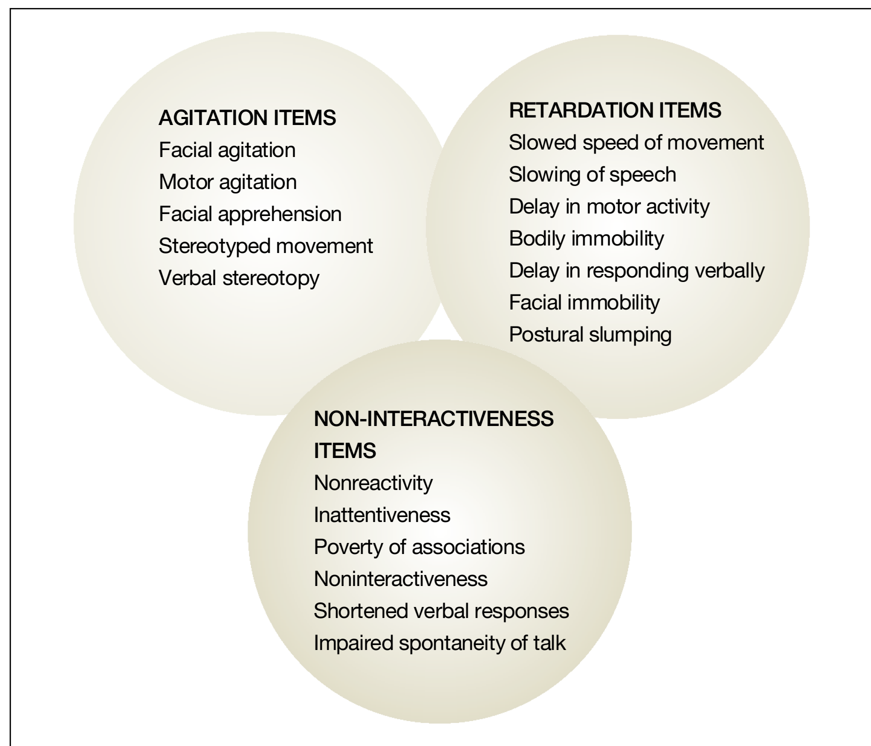

Figure 1. The elements of psychomotor disturbance that are assessed in the CORE assessment of psychomotor change.

Diagnosis and assessment of melancholic depression

Establishing a diagnosis of melancholic depression in a patient with an episode of depression of clinical significance involves both of the following:

- identifying symptoms related to melancholic depression (that is, anhedonia, non-reactivity, diurnal mood variation and early morning wakening), and
- observing psychomotor disturbance involving retardation and/or agitation in association with impaired cognitive processing (poor concentration and inattention).

A suggested hierarchy of questions to ask patients is outlined in Table 2.

The CORE rating scale can be used to assess psychomotor retardation. This tool comprises 18 signs (observable features) that are rated by the clinician or a trained observer at the end of a clinical interview. Summing subsets of the items produces scores on three dimensions found to underlie psychomotor change: noninteractiveness, retardation and agitation (Figure).[9] The timing of use of the rating scale should take into consideration the presence of diurnal mood variation, as the signs may fluctuate over the day. Further information about the CORE system is available at the Black Dog Institute website (see the box on page 24). Family members often report significant changes in behaviour in patients with melancholic depression. These changes include change in tone

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Website resources for GPs and patients

Beyondblue

The beyondblue website is http://www.beyondblue.org.au
Downloadable fact sheets and resources for health professionals are available from:
http://www.beyondblue.org.au/index.aspx?link_id=7.102
Downloadable information resources for patients are available from:
http://www.beyondblue.org.au/index.aspx?link_id=7.980

Patient information

- Medical treatment – http://www.beyondblue.org.au/index.aspx?link_id=89.581
- Antidepressants – http://www.beyondblue.org.au/index.aspx?link_id=89.581
- Depression and dementia. Fact sheet 25 – http://www.beyondblue.org.au/index.aspx?link_id=89.585&tmp=FileDownload&fid=930
- Helping yourself – http://www.beyondblue.org.au/index.aspx?link_id=89.586

Black Dog Institute

The Black Dog Institute website is http://www.blackdoginstitute.org.au
Downloadable information sheets, fact sheets and other resources, including a list of self-help books, for health professionals and patients are available from:
http://www.blackdoginstitute.org.au/healthprofessionals/resources/overview.cfm

GP resources mentioned in article

- **The CORE rating sheet and booklet.** The observable psychomotor signs of melancholic depression can be rated using the CORE rating sheet. This and an explanatory booklet are available at: http://www.blackdoginstitute.org.au/docs/2.COREAssessmentScoringSheet.pdf and http://www.blackdoginstitute.org.au/docs/COREbooklet.pdf
- **A rational model for antidepressant drug prescription.** A GP information sheet about prescribing antidepressants for various depression types. Available at: http://www.blackdoginstitute.org.au/docs/arationalmodelforantidepressantdrugprescription_000.pdf
- **An integrative depression model** and **Understanding your depressive episode.** An assessment and management tool, including a sheet for patients and doctors to collaborate on. Available at: http://www.blackdoginstitute.org.au/docs/UnderstandingYourDepressiveEpisode_000.pdf
- **Relapse signature: learning from experience.** Patient handout. Available at: http://www.blackdoginstitute.org.au/docs/18.RelapseSignatureLearningfromExperience.pdf

Patient information

- Melancholic depression – http://www.blackdoginstitute.org.au/public/depression/depressionexplained/types.cfm#Melancholic
- Bipolar depression – http://www.blackdoginstitute.org.au/public/bipolardisorder/bipolardisorderexplained/ bipolardepression.cfm
- Treatments for depression – http://www.blackdoginstitute.org.au/public/depression/treatments/index.cfm
- Depression in teenagers and young adults – http://www.blackdoginstitute.org.au/public/depression/inteenagersyoungadults.cfm
- Depression in the over-65 age group – http://www.blackdoginstitute.org.au/public/depression/inover65s.cfm
- The book *Dealing with Depression: a Common Sense Guide to Mood Disorders,* 2nd edition, by Professor G Parker and published by Allen and Unwin, Sydney in 2004 (http://www.blackdoginstitute.org.au/aboutus/blackdogbooks.cfm).

Table 3. Red flags for melancholic depression

- Sudden and significant change in behaviour, leading to social withdrawal, onset of intense agitation and/or panic; this is often noted by relatives and may have a diurnal pattern
- Poor sleep (middle or late insomnia), early morning waking (around 3 a.m.)
- Sudden unexplained appetite loss, with significant weight loss, constipation
- Sudden inability to work effectively, complaints about being unable to think
- Unusual ruminations/preoccupations (fatal illness, no money, past misdeeds and failures); there may be some justification for the concerns but the levels of concern and preoccupation are completely out of proportion
- Talk of hopelessness, ‘no point to life’

of voice, loss of ‘light in their eyes’, and changes in posture, gait, speed of movement and speech. It is also worth noting that patients with good social skills may underplay their inner distress and despair by maintaining a veneer of good manners (‘Don’t worry about me’, ‘Other people need you more’, ‘I’ll be alright’).

Red flags for melancholic depression are listed in Table 3.

Management of melancholic depression

It can be very wearing being with someone with a melancholic depression because he or she may be cognitively slowed, self-deprecatory and demanding frequent reassurance. Those patients who are agitated and psychotic may be particularly taxing; the family are often frightened about the change in their loved one. This may be

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An overview of drugs commonly used in managing patients with depression

Antidepressants

- **Selective serotonin reuptake inhibitors (SSRIs).** SSRIs are narrow-action antidepressants, having an effect only on serotonin reuptake. SSRIs available in Australia are citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine and sertraline.*
- **Serotonin and noradrenaline reuptake inhibitors (SNRIs).** SNRIs are dual-action antidepressants, having both serotonergic and noradrenergic effects. SNRIs available in Australia are desvenlafaxine, duloxetine and venlafaxine.*
- **Tricyclic antidepressants (TCAs).** TCAs are also dual-action antidepressants, blocking the reuptake of serotonin and noradrenaline. They are less often used nowadays because more selective and safer drugs are available, but they are still appropriate to use in severe cases of major depression because of their effectiveness. Imipramine and nortriptyline are considered as the less sedating TCAs, and amitriptyline, dothiepin, doxepin and trimipramine as the more sedating TCAs.*
- **Noradrenergic and specific serotonergic antidepressants (NaSSAs).** The NaSSAs mianserin and mirtazapine (the 6-aza analogue of mianserin) are dual-action antidepressants.* The main side effects of mirtazapine are drowsiness and weight gain and it is therefore of use when a more sedating antidepressant is needed, such as when there is significant anxiety or insomnia. Mianserin is also of use for its sedating properties.
- **Noradrenaline reuptake inhibitors (NRIs).** NRIs have a positive effect on concentration and motivation in particular. Reboxetine is of use when an antidepressant with a stimulating effect is required.*
- **Noradrenaline–dopamine reuptake inhibitors (NDRIs).** As well as having antidepressant effects, the NDRI bupropion also acts as a nicotine-receptor antagonist. Its antidepressant effect is considered to be mediated by its dopaminergic and noradrenergic action. Its antismoking effects are thought to be due to a combination of its noradrenergic, dopaminergic and nicotine-receptor blockade effects in attenuating the effects of nicotine withdrawal. It is also of use in other substance withdrawal. Bupropion is not indicated on the TGA for depression, but is indicated as an aid for smoking cessation.*
- **Monoamine oxidase inhibitors (MAOIs).** MAOIs prevent the breakdown of the monoamine neurotransmitters serotonin, noradrenaline and dopamine. Moclobemide, a reversible inhibitor of monoamine oxidase A (RIMA), is shorter-acting than the older MAOIs such as phenelzine and tranylcypromine but generally not as effective in depression.* Phenelzine and tranylcypromine have significant side effects because of their irreversibility, and should be initiated by a psychiatrist.

Antipsychotics, mood stabilisers and antianxiety agents

- **Typical antipsychotics.** First-generation antipsychotics; examples are chlorpromazine, haloperidol and trifluoroperazine.*
- **Atypical antipsychotics.** Second-generation antipsychotics; examples are olanzapine, quetiapine and risperidone.* Olanzapine and quetiapine have mood-stabilising effects.
- **Lithium.** Lithium is an antipsychotic with mood-stabilising effects (it is TGA indicated for mania).*
- **Sodium valproate**. Sodium valproate is an anticonvulsant and antipsychotic with mood-stabilising effects (it is TGA indicated for mania).*
- **Lamotrigine.** Lamotrigine is an antiepileptic with mood-stabilising effects.*
- **Benzodiazepines.** Diazepam is an example of an anxiolytic benzodiazepine.

* TRADE NAMES: Atypical antipsychotics: olanzapine – Zyprexa; quetiapine – Seroquel; risperidone – Rispa, Risperdal, Rixadone. MAOIs: moclobemide – Amira, Aurorix, Clobemix, Maosig, Mohexal; phenelzine – Nardil; tranylcypromine – Parnate. NaSSAs: mianserin – Lumin, Tolvon; mirtazapine – Avanza, Avanza SolTab, Axit, Mirtazon, Remeron. SNRIs: desvenlafaxine – Pristiq; duloxetine – Cymbalta; venlafaxine – Efexor-XR. SSRIs: citalopram – Celapram, Celica, Ciazil, Cipramil, Citalobell, Talam, Talohexal; escitalopram – Esipram, Lexapro; fluoxetine – Auscap 20 mg Capsules, Fluohexal, Fluoxebell, Lovan, Prozac, Zactin; fluvoxamine – Faverin, Luvox, Movox, Voxam; paroxetine – Aropax, Extine, Paxtine; sertraline – Concorz, Eleva, Sertra, Setrona, Xydep, Zoloft. TCAs: amitriptyline – Endep; dothiepin – Dothep, Prothiaden; doxepin – Deptran, Sinequan; imipramine – Tofranil, Tolerade; nortriptyline – Allegron; trimipramine – Surmontil. Typical antipsychotics: chlorpromazine – Largactil; haloperidol – Serenace; trifluoroperazine – Stelazine. Other drugs: bupropion – Clorprax, Prexaton, Zyban SR; diazepam – Antenex, Ducene, Ranzepam, Valium, Valpam; lamotrigine – Elmendos, Lamictal, Lamidus, Lamitrin, Lamogine, Seaze; lithium – Lithicarb, Quilonum SR; reboxetine – Edronax; sodium valproate – Epilim, Valpro.

especially so if any other family members have had a serious mood disorder.

Information sheets about depression and caring for a person who is depressed are available on the beyondblue and Black Dog Institute websites (see the box on page 24).

Pharmacological management

Although selective serotonin reuptake inhibitors (SSRIs; citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline) may be sufficient in patients with initial episodes and those without pronounced psychomotor change, the dual-acting antidepressants, the serotonin and noradrenaline reuptake inhibitors (SNRIs; desvenlafaxine, duloxetine, venlafaxine) are likely to be the most appropriate class of antidepressant drug to use in the management of melancholic depression. If there is no improvement on

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Choosing antidepressants – the Black Dog Institute model*

The Black Dog Institute, Sydney, has developed a model for a rational approach to the choice of antidepressant drugs.[10] Although speculative, the model has been supported by a number of effectiveness studies.

In this model, the various types of depression are thought to have different aetiological processes, and the ratios of the neurotransmitters serotonin, noradrenaline and dopamine associated with each depression are different. The neurotransmitter serotonin is involved in all depressions and is the main neurotransmitter implicated in nonmelancholic disorders, while it is thought that noradrenaline plays a more important role in melancholic depression, and that dopamine is also important in psychotic depression.

Targeting the neurotransmitter(s) associated with a particular depression type guides antidepressant choice.

- **Nonmelancholic depression.** The associated neurotransmitter is serotonin, so use a narrow-action (serotonergic) antidepressant: a selective serotonin reuptake inhibitor (SSRI).
- **Melancholic depression.** The associated neurotransmitters are serotonin and also noradrenaline, so use a dual-action (serotonergic and noradrenergic) antidepressant. Start with a serotonin and noradrenaline reuptake inhibitor (SNRI); if no response, trial a tricyclic antidepressant or mirtazapine.
- **Psychotic depression.** The associated neurotransmitters are dopamine and also noradrenaline and serotonin, so use a broad-action antidepressant strategy. This may be achieved by the prescription of a dual-action antidepressant plus an antipsychotic drug (for its dopaminergic activity).

Each antidepressant agent can have its profile 'broadened' by augmentation with an atypical antipsychotic, most of which have dopaminergic and serotonergic activities.

* 'A rational model for antidepressant drug prescription.' http://www.blackdoginstitute.org.au/docs/arationalmodelforantidepressantdrugprescription_000.pdf

using the SNRIs, the tricyclic antidepressants (TCAs; amitriptyline, dothiepin, doxepin, imipramine, nortriptyline, trimipramine), which are also dual-action antidepressants, should be considered next. The drugs commonly used in the management of patients with depression are discussed in the box on page 25.

The rationale for these drug choices is that episodes that are later onset, more complex in terms of medical and psychiatric comorbidity and are recurrences are more likely to have psychomotor change, which is thought to also involve noradrenergic systems. Psychotic symptoms are more evident in older people and those with bipolar disorder, stimulant abuse or significant family history of psychosis, and are thought to also involve dopaminergic systems. This is explained in the information sheet 'A rational model for antidepressant drug prescription', available on the Black Dog Institute website and summarised in the box on this page.[10]

It is expected that GPs will consult a psychiatrist in most cases of melancholic depression, particularly if the depression is first onset, complex and/or associated with prominent psychomotor signs, suicidal ideation or psychosis. The steps below illustrate the likely sequence of antidepressant use in patients with melancholic depression.

- If no previous medication or episodes:
  – Step 1: if younger onset or no distinct psychomotor disturbance change, start with an SSRI; if older onset or distinct psychomotor disturbance, start with a dual-action antidepressant (an SNRI)
- If the SSRI failed or improvement is only partial, or there was lack of response to SSRIs on previous occasions, go straight to:
  – Step 2: an SNRI; then, if there is no improvement, trial a TCA
  – Step 3: psychiatrists may consider other medications, such as a monoamine oxidase inhibitor (MAOI; usually phenelzine), or electroconvulsive therapy.

A model for the management of acute unipolar melancholic depression is outlined by Professor Gordon Parker and Dr Vijaya Manicavasagar in their book *Modelling and Managing the Depressive Disorders: a Clinical Guide.*[4]

Notes on antidepressant use

- Consider target symptoms, past history, risk of overdose, medical history, current medications and past sensitivities and interactions.
- The superiority of TCA over SSRI antidepressants increases with patient age but their use needs to be considered against possible cardiac risk factors.
- If an antidepressant alone fails, brief augmentation with an antipsychotic may 'kick-start' response. Possible augmentation strategies include lithium, olanzapine or another antipsychotic at each step. Antipsychotic medications may also have mood-stabilising properties.
- If there is evidence of anxiety, use a more sedating antidepressant (e.g. mirtazapine, some TCAs [small doses of amitriptyline, dothiepin, doxepin and trimipramine]) or a short course of a benzodiazepine such as diazepam.
- If there is evidence of agitation, anticipate the presence of psychotic symptoms and use a sedating

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antipsychotic agent such as olanzapine, quetiapine or chlorpromazine. Use risperidone if less sedation is required. If the patient becomes more agitated on treatment, it is worth considering the presence of akathisia or the syndrome of inappropriate antidiuretic hormone secretion, particularly in older people or those on multiple medications.
- Patients with agitation and/or psychotic symptoms generally require an antipsychotic agent from the start of treatment. Urgent psychiatric support should be enlisted.
- If there is evidence of bipolar disorder, the patient should be observed closely as prescription of an antidepressant may 'switch' him or her into a manic episode.
- In a younger person with a first or early episode of melancholic depression, it is worth being wary of precipitating a first manic episode.
- It is best to consult a psychiatrist and/or mental health team and use a mood stabiliser (e.g. lithium, sodium valproate, lamotrigine or an atypical antipsychotic such as olanzapine) concurrently with an antidepressant.
- When patients become extremely agitated, stop eating and drinking or consider suicide based on delusional beliefs of guilt, the situation constitutes an emergency and requires urgent psychiatric attention.

Psychosocial management

In addition to a severe mood disorder, patients with melancholic depression may have a reversible cognitive impairment affecting thinking speed, reasoning and judgement. They should be discouraged from making major decisions while depressed.

Family members are often worried and frightened by the changes that melancholic depression brings to their loved ones. It is important to educate and support the family as much as possible.

Patients should be encouraged to participate in as much activity as possible. This can involve gentle exercise and some scaled down pursuit of regular interests. If there is marked diurnal mood variation, it may be possible to schedule some activities for the part of the day when the patient is more motivated (usually in the afternoon and evening).

Although melancholic and psychotic depressions are largely 'biologically driven', there are often stressors that require attention. With early-onset melancholia, there is a need to review the experience, consider the family history, talk about ensuring good sleep and diet, educate about keeping away from substances and discourage smoking, as these will have profound effects on disease burden if the patient goes on to have repeated episodes of depression and/or bipolar disorder. It is often a time when family secrets are revealed (such as other family members with depression or who have attempted suicide), and these need to be dealt with sensitively. With late-onset depression, there is a need to ensure a healthy lifestyle to help decrease cardiovascular risk factors and maintain healthy blood pressure, observe cognitive function and address psychosocial issues related to ageing.

Factors complicating recovery

Slow recovery from an episode of melancholic depression may be an indication that there are factors complicating the recovery. It can be worth checking for factors such as those listed below, some of which may only emerge after the diagnosis has been made:

- comorbid alcohol, substance, analgesic and/or sedative abuse or dependence; nicotine dependence
- medical illness, including endocrine disorder, malignancy, respiratory disease and renal disease – either previously known or became apparent during episode
- medication use – such as sedatives, analgesics, corticosteroids
- microvascular disease and/or other degenerative process including evolving dementing process and Parkinson's disease
- 'unfinished emotional business' – especially grief and anger
- psychotic symptoms – not as bizarre as in schizophrenia, and may go unrecognised; these should always be suspected in the presence of agitation.

Reappraisal further down the track

When in the depths of a melancholic depressive episode, a patient may be unable to articulate any current problems because their mood state is so overwhelming. On recovery from the episode, it is important to 'have another look' at the patient to reassess any biological or personality vulnerability that can be improved to reduce the risk of future relapse or recurrence. This can be done by asking the questions, 'Why this person?' and 'Why now?'. The 'Understanding your depressive episode' worksheet on the Black Dog Institute website can be completed with a patient as a way of making sense of the vulnerabilities and precipitants of depressive episodes in that individual.

It is worth considering whether there are any personality/temperamental vulnerabilities to address after a patient has recovered from an acute episode (see the second article in this supplement).[2]

For patients with a younger age of onset, constructing a family tree over previous generations can reveal recurrent depression, bipolar disorder, psychotic illness or deliberate self-harm in relatives. For older-onset depression, the emphasis is more on a family history of vascular disease or other neurodegenerative disease, such as dementia.

Anticipating relapse

It is also worth making a relapse plan, noting any characteristic 'relapse signature'. Rather than frighten the patient by talking of more episodes, this can be done by working out what can be learned from

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the episode, and what could be done differently next time. A patient handout about the relapse signature is available on the Black Dog Institute website.

A watchful presence of patients should be maintained after recovery. Follow-up at regular intervals (say, six-monthly) should be considered to check general health, note any changes in mood and psychomotor disturbance and reinforce healthy lifestyle messages.

Conclusion

Melancholic depression, whether it is of early or late onset, is associated with significant morbidity and high suicide risk.

Diagnosis relies on the identifying of symptoms such as anhedonia, non-reactivity, profound lack of motivation, cognitive difficulties, diurnal mood variation and early morning wakening, and on observing specific features of psychomotor disturbance indicating non-interactiveness, retardation and agitation. Comorbid alcohol, substance, analgesic and/or sedative abuse or dependence, nicotine dependence, medical illness, medication use, microvascular disease, other degenerative processes, 'unfinished emotional business' and psychotic symptoms may complicate the course of the depression.

Antidepressants are generally required for patients with melancholic depression, and antipsychotics may also be needed. Patients with associated psychotic features will require both antidepressants and antipsychotics.

The Black Dog Institute and beyondblue websites have many downloadable resources for both health professionals and patients on all aspects of depression. MT

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COMPETING INTERESTS: Professor Wilhelm has written material for GP workshops on depression-related topics and also resources that appear on the Black Dog Institute website.

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W20091274 AP17011 Production date: 01 January 2010

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