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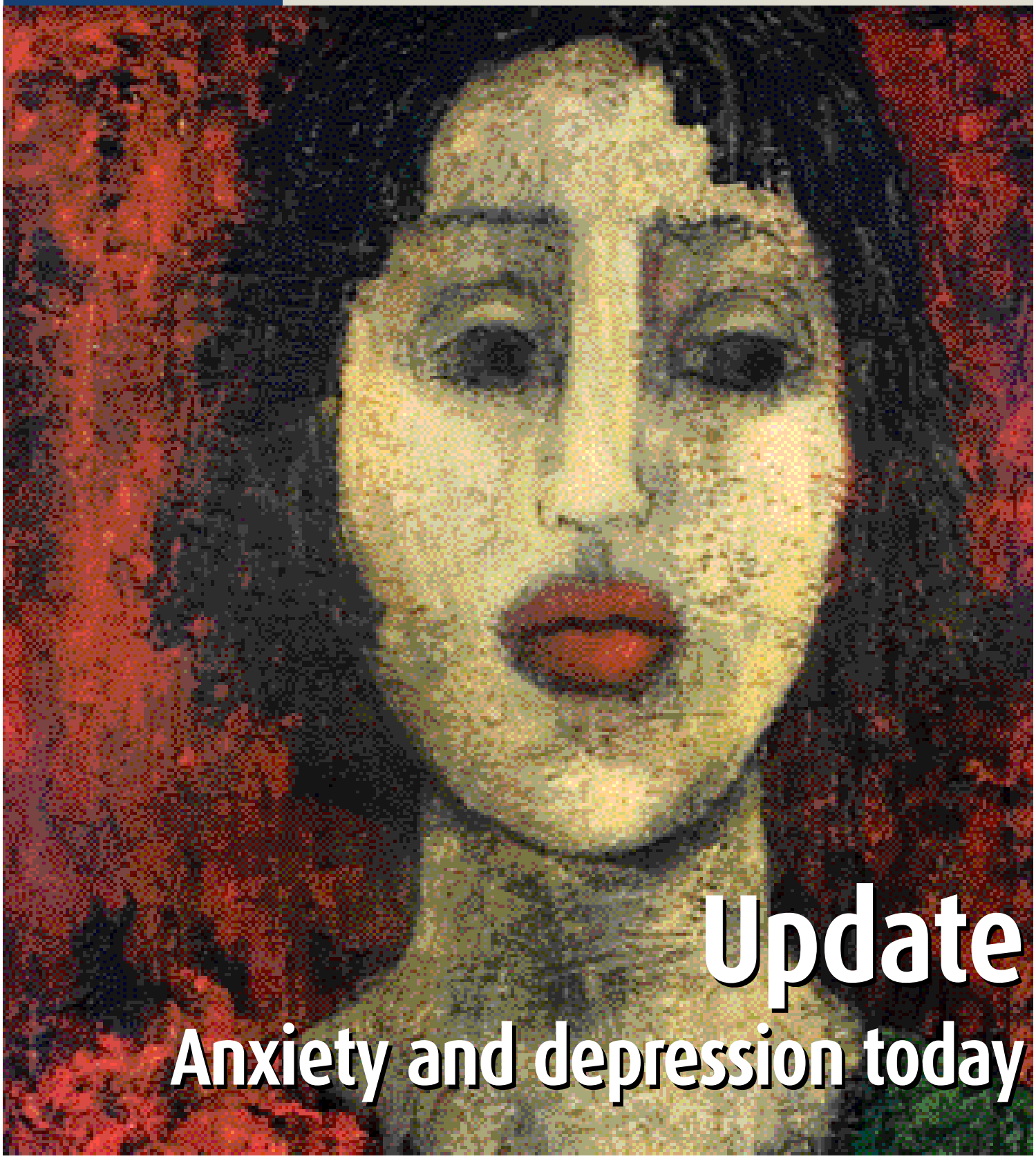

Update

Anxiety and depression today

UPDATE: ANXIETY AND DEPRESSION TODAY
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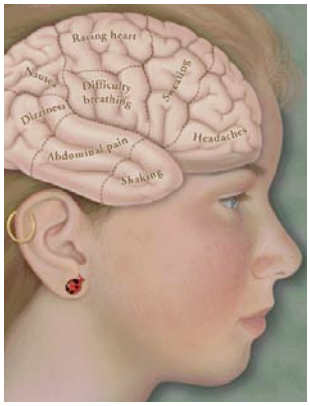

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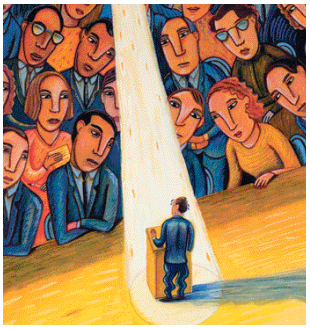

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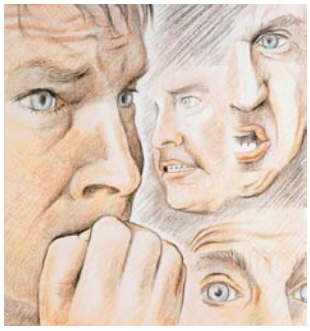

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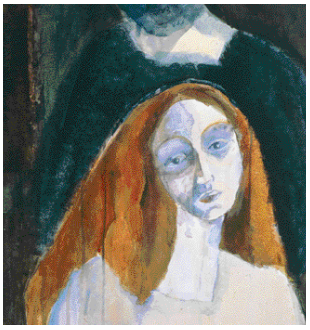

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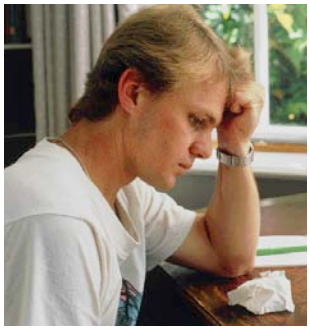

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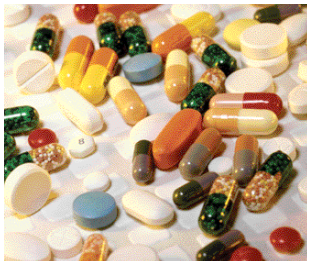

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Treating anxiety and depression in Australia

Reasons for optimism

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It will come as no surprise to the GP reader of this *Medicine Today* supplement that depression and anxiety comprise two of the most common and disabling conditions for the Australian community. In any single year, about 6% of the Australian population will experience an episode of major depression and about 10%, an anxiety disorder.

Moreover, these conditions are disproportionate causes of impaired functioning. Depression comprises more than 10% of total illness-related disability, and is projected to become the second leading cause of disease burden (an index combining both disability and premature death) worldwide by 2020. Furthermore, depression is the main cause of suicide, accounting for at least 60% of cases.

The GP is at the vanguard of diagnosis and treatment for these conditions. Psychological disorders comprise a large proportion of problems presenting to GPs, with about 10 to 20% of primary care patients having either primary or substantial mental health issues. About 85% of antidepressants in Australia are prescribed by GPs, with most prescriptions being initiated in primary care.

Enhanced general practice care

Whereas 10 to 15 years ago, GPs were being lambasted by their specialist colleagues for underrecognition and undertreatment of depression and anxiety, the situation has reversed dramatically in the intervening period, with the diagnosis and management of depression in particular improving dramatically.

Several factors have probably contributed. New antidepressant medications (such as the SSRIs) and targeted short term psychological interventions (such as problem solving techniques and cognitive behavioural therapy) have been developed that are regarded as both acceptable and applicable in the primary care setting. The Commonwealth national depression initiative *beyondblue* has greatly enhanced public awareness of depression and anxiety and contributed substantially to reducing the stigma associated with these conditions. The 'coming out' of high profile Australians with depression and anxiety, such as actor Gary McDonald and politician Geoff Gallop, has made enormous inroads into 'normalising' these disorders as genuine health concerns. The Commonwealth Better Outcomes in Mental Health Care program has enhanced GP diagnostic and treatment skills and enabled greater access to specialised psychological care. Furthermore, the Medicare funding for clinical psychologists heralded in the recent Council of Australian Governments' mental health announcements will further increase availability of psychological treatments.

Benefits becoming evident

Encouragingly, there is growing evidence in Australia and other Western countries that the increased treatment of depression is finally paying dividends in terms of reducing rates of suicide, the ultimate tragic outcome of this disorder. This is predominantly a reflection of the improved care in general practice.

So there are substantial reasons for optimism that the improvements in diagnosis, treatment and service provision of depression and anxiety are at last translating into benefits at both the individual patient and population level. The articles in this supplement will further enhance your skills in assisting your patients with these common, distressing and disabling conditions. MT

Managing anxiety disorders in children and adolescents

A child or adolescent presenting with school refusal, physical symptoms like headaches or stomach aches, or speech problems may have an anxiety disorder.

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Anxiety disorders are among the most common psychiatric disorders affecting children and adolescents. While figures vary, the rate of these disorders is thought to be around 9%.[1] Despite this high rate and the significant impairment that anxiety disorders cause, they are highly treatable, with a growing evidence base supporting the safety and effectiveness of treatments such as cognitive behavioural therapy (CBT), family therapy and medication.

Anxiety and anxiety disorders

Anxiety is a normal and useful emotion important in maintaining safety and improving performance. Specific anxieties are part of normal child development, such as separation anxiety in infants and young toddlers. Anxiety disorders are not simply too much anxiety; rather they are developmentally inappropriate concerns characterised by irrational fears and the avoidance of situations associated with these concerns. Anxiety disorders lead to impairment of day-to-day functioning and prolonged and intense distress.

Children and adolescents are prone to the same anxiety disorders as adults but the various disorders tend to present first at different ages. In children, the most common anxiety disorders are separation anxiety disorder, selective mutism and post-traumatic stress disorder (PTSD). In adolescents, the most common are generalised anxiety disorder, social phobia, agoraphobia and panic disorder.

When faced with feared situations, children may experience physical symptoms such as a racing heart, difficulty breathing, nausea, dizziness, sweating and shaking. These symptoms resolve rapidly once the child is away from the feared situation, which indirectly encourages avoidance.

One-third of all children presenting with anxiety disorders will have two or more such disorders, and one-third will also have a major depressive disorder.

IN SUMMARY

- **Anxiety disorders are among the most common psychiatric disorders affecting children and adolescents.**
- **Untreated anxiety disorders in children and adolescents are associated with high rates of impairment in educational and social development during adolescence, and with adult anxiety disorders, substance abuse, unemployment and social isolation.**
- **Anxiety disorders are highly treatable with psychological therapies (including cognitive behavioural and family therapy) and antidepressant medications.**
- **Common anxiety presentations in children and adolescents include separation anxiety with school refusal and somatisation (headaches, abdominal pain), anxiety about school performance and social anxiety.**

Causes of anxiety disorders

While the exact cause of anxiety disorders remains unknown, we do know that genetics and environment both play a role. Studies of families have shown that children with anxiety disorders are much more likely to have parents or siblings with anxiety disorders. In adults, twin and adoption studies have confirmed a strong genetic contribution to anxiety disorders. It is, however, the tendency towards anxiety that is inherited rather than specific anxiety disorders, and this tendency responds to, and is shaped by, life experiences.

Types of anxiety disorders

Separation anxiety disorder

Separation anxiety disorder is the most common anxiety disorder in children, with rates of between 2.4 and 4.7%, mainly in the under-12s. This type of anxiety affects both sexes equally, and the most common age of onset is 6 to 8 years.[2]

Separation anxiety disorder is characterised by excessive fears about being apart from those people most important to the child. The primary fear for affected children is that harm may come to their carers or themselves. For example, children fear that their parents may become the victims of an accident or a murder.

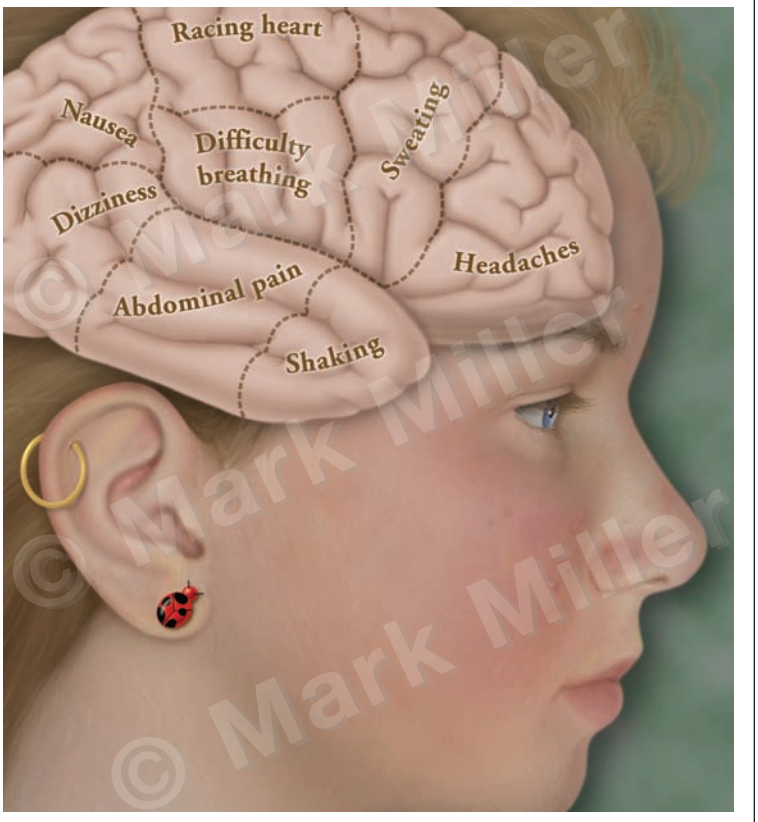
Children with separation anxiety disorder are often unable to go to school, stay at friends' homes, attend school camps, or even sleep alone. They complain of nightmares and often have multiple physical complaints, including headaches and stomach aches. Nearly three-quarters of children with separation anxiety disorder have associated school refusal.[2]

Generalised anxiety disorder

Generalised anxiety disorder, previously known as overanxious disorder, is the second most common anxiety disorder of children, with rates ranging from 2.9 to 4.6%.[3] It is characterised by excessive worrying about future events, social acceptability, personal adequacy and competency.

Children with generalised anxiety disorder often appear overly mature, attempting to carry out tasks and responsibilities perfectly. They regularly seek reassurance for their worries and doubts, are overly sensitive to criticism and frequently present with a variety of physical symptoms.

Anxiety disorders in children and adolescents



Anxiety disorders affect almost one in 10 children and adolescents, and may cause significant impairment and distress. Fortunately these disorders respond well to cognitive behavioural therapy and medications. Selective serotonin reuptake inhibitors are the medications of choice.

Social phobia

Social phobia, which was previously known as avoidant disorder in children, affects around 1.0% of children and adolescents.[1] It is characterised by avoidance of social or performance situations for fear of being negatively judged or doing something embarrassing. While some children may have very specific fears, such as eating or writing in public, most will fear many different types of social situations. Commonly feared situations include public speaking or performing (such as reading in class), social gatherings and interactions with strangers. Untreated social phobia has a high association with substance abuse in late adolescence and adulthood.

Table. Cognitive behavioural therapy

Central beliefs of CBT

- Thoughts influence behaviours and feelings
- Unhelpful thoughts generating anxiety can be identified and challenged
- By replacing these unhelpful thoughts with more realistic ones, behaviours and feelings can be changed.

CBT interventions for anxiety

- Relaxation
- Slow breathing to control panic symptoms
- Graded exposure to anxiety provoking situations
- Problem solving
- Social skills
- Assertiveness training
- Cognitive restructuring (challenging anxious thoughts)

Post-traumatic stress disorder

Made famous in Vietnam War movies, PTSD is also seen in children exposed to a variety of life threatening or potentially life threatening events. Exposure is usually but not always unexpected. In Australia and similar countries, exposure to chronic abuse or domestic violence is a common cause of PTSD, and similarly for children in war zones exposure to trauma is often expected.

PTSD involves the constant reliving of the traumatic event and avoidance of similar situations. Children with PTSD experience nightmares, recurrent intrusive thoughts and flashbacks. They are chronically overaroused, reacting to situations of even minor threat with either explosive rage or complete shutdown.

Events leading to PTSD in children include physical and sexual abuse and domestic violence and also witnessing of house fires, natural disasters such as bushfires, and vehicle accidents. The more severe the event, the more likely someone is to develop symptoms. However, some individuals develop symptoms after minor trauma and others do not develop symptoms despite exposure to major trauma.

Selective mutism

Selective mutism is characterised by the absence of speech in specific situations and the presence of speech in others. The condition is similar in many ways to social phobia but is less common. Community studies have identified rates of this disorder of 0.1%, mainly affecting younger children who often are from bilingual backgrounds.[4] Affected children tend to be reluctant to speak to strangers and when they are in places away from the family home, such as at school. Transient selective mutism is often seen in children when they start school (0.71%).[5]

Treating anxiety disorders

The treatment of child and adolescent anxiety disorders falls into two broad categories: psychological therapies and medication management.

Cognitive behavioural therapy

CBT is the psychological therapy best supported by studies, and is regarded as the first line treatment of anxiety disorders in children and adolescents. It is a talking based therapy arising from the link between thoughts, feelings and behaviour. The central beliefs of CBT and interventions for anxiety are listed in the Table. CBT in children can take place in a group setting or on an individual basis, with or without parental involvement.

Randomised controlled trials of the use of CBT in the treatment of social phobia, generalised anxiety disorder and separation anxiety disorder have shown CBT to be significantly superior to no treatment in the management of these conditions.[6-9] These trials, of 12 to 16 weeks' duration, involved either individual or group therapy. Three compared child-only CBT with parent and child CBT and demonstrated a probable advantage in the involving of parents.[7-9]

Family therapy

Family based interventions in childhood anxiety disorder have focused on parents and children participating together in CBT. Parental participation enables the parents, particularly those of younger children, to develop an understanding of their child's illness as well as learn strategies to assist their child during anxious episodes. Also, since CBT needs regular practice of intervention strategies (often referred to as homework), involving parents helps maintain children's motivation, thus maximising outcomes. Parental involvement has been shown to be beneficial in maintaining remission over time, particularly in families where parents themselves are anxious.[9]

Selective serotonin reuptake inhibitors

Selective serotonin reuptake inhibitors (SSRIs) are the medications of choice for treating anxiety disorders in children and adolescents because of their demonstrated efficacy and safety.

Since 1990 there have been four double-blind randomised placebo-controlled trials of SSRIs in children and adolescents.[10-13] These trials involved 242 children with a range of anxiety disorders, and showed fluoxetine, sertraline and fluvoxamine to be significantly superior to placebo, and that these drugs were well tolerated and safe.

Choosing an SSRI

Concerns have been raised recently about a link between SSRIs and suicidal behaviour. This concern has been highlighted in the use of SSRIs for depression in children and adolescents; however, the link remains controversial and questionable. No suicides have been recorded among more than 2000 children involved in randomised controlled trials of SSRIs in the treatment of depression. Additionally,

no trial has shown a statistically significantly higher rate of suicidal ideation in children treated with SSRIs compared with those treated with placebo. To date, no link has been shown between SSRI use in the treatment of anxiety in children and adolescents and suicidal ideation or behaviour.[14]

Most evidence exists for the efficacy of fluoxetine (Auscap, Fluohexal, Fluoxebell, Lovan, Prozac, Zactin) in the treatment of depression and anxiety. As previously mentioned, there is also evidence of the efficacy of sertraline (Concorz, Eleva, Xydep, Zoloft) and fluvoxamine (Faverin, Luvox, Movox, Voxam) in this group of disorders. The main differences between these medications are in their half-lives and preparations. Fluoxetine has a half-life of up to two weeks compared to one day or less for sertraline and fluvoxamine, which is particularly useful in adolescents where medication is often missed or forgotten. Also, fluoxetine is available in a liquid form (Lovan), allowing small doses to be more simply given.

SSRI dosages and side effects

Up to 80% of children and adolescents prescribed SSRIs will experience mild transient side effects, the most common being abdominal discomfort, headache and sleep disturbance. While most side effects settle within three to four days, up to one in 12 children will experience behavioural agitation or hypomania necessitating cessation of medication. These complications can be minimised by using low starting doses of medication, with gradual increases as needed.

Generally, most adolescents would start on half the normal adult starting dose of an SSRI and prepubertal children would start on one-quarter. In most adolescents, the dose will need increasing to a standard adult dose. As in adults, SSRIs are not lethal in overdose in children and adolescents.

Two other important side effects in children and adolescents taking SSRIs are sexual dysfunction and withdrawal symptoms on medication cessation. Sexual dysfunction in adolescents taking SSRIs is a clinically significant phenomenon, particularly in young males who are unlikely to remain compliant with medication or discuss this problem should it occur.

Withdrawal phenomena are experienced with rapid cessation of SSRI treatment, and include agitation, restlessness, poor concentration, fatigue and insomnia. Also of concern is the possible increased risk of relapse associated with rapid cessation. Ceasing medication over a two-week period reduces withdrawal symptoms.

Concurrent medical illness

In general, SSRIs are safe in chronically medically ill patients. They are largely metabolised by the liver and their metabolites are excreted by the kidneys. Dosages should, therefore, be reduced in children and adolescents with renal and liver impairment. Theoretically, SSRIs may marginally decrease seizure threshold, but in practice this is not a significant consideration in patients with epilepsy. These medications have no impact on cardiac conduction, heart rate or blood pressure.

Tricyclic antidepressants

There have been five double-blind randomised controlled trials of tricyclic antidepressants (TCAs) in child and adolescent anxiety disorders since 1970, all in children with school refusal.[15] Only two of these trials showed TCAs to be significantly superior to placebo.

As evidence for the efficacy of TCAs remains equivocal, they are at best a second-line treatment for childhood anxiety disorders, with use confined to specialist clinics. This is particularly so given that TCAs have been associated with seven unexplained sudden deaths in the USA and are potentially lethal in overdose.

Benzodiazepines

There have been four controlled trials of benzodiazepines in children and adolescents with anxiety, and these involved either clonazepam or alprazolam.[16,17] These trials have not demonstrated a significant difference between benzodiazepines and placebo. Given the problems of sedation, dependence, tolerance and withdrawal associated with benzodiazepine use, there is little role for these drugs in the treatment of child and adolescent anxiety.

Conclusion

Anxiety disorders are common in children and if left untreated may persist into adolescence and adulthood. They respond well to treatment and the evidence is accumulating that CBT and medication can be helpful. There is a tendency for affected children not to present with anxiety but with school refusal, physical symptoms and sometimes speech problems.

Anxiety disorders can also be anxiety provoking for doctors if we are unfamiliar with the treatments available. Treating anxiety in childhood is both rewarding and valuable in the long term for helping prevent the problems the condition can cause in later life. MT

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Assessing and treating mixed depression and anxiety

How can clinicians make sense of patients experiencing both depression and anxiety, and decide on treatment? This article reviews the overlap between depression and the various anxiety disorders and details the various pharmacological and psychological therapeutic options.

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The co-occurrence of depression and anxiety is common in clinical practice. The Australian National Survey of Mental Health and Well-Being found that in the 12 months prior to interview, 5.8% of the adult population had major depression and 9.7% an anxiety disorder.[1] However, depression alone accounted for only 1.4% of the population and an anxiety disorder alone only 2.9%. Significantly, over 3% reported mixed anxiety and depression. These figures indicate that such mixed presentations are more common than 'pure' presentations of anxiety or depression – a fact well known to experienced clinicians.

Why does it matter whether depressed patients are anxious, or vice versa? The major reason is that such comorbidity is generally associated with more severe illness. Patients with comorbid depression and anxiety (e.g. generalised anxiety disorder, panic disorder, etc) are less treatment responsive, are more functionally impaired and disabled, have a higher suicide risk, and are slower to respond to treatment.[2]

The increased disabling effect can be seen, for example, in data from the Australian National Survey. The average 'days out of role' in the prior 12 months due to the combination of anxiety and depression was 3.6, compared with 2.1 days for anxiety alone and 2.7 for depression.[1]

How to approach the mixed presentation

We recommend that the most clinically useful approach to deciding on treatment for patients with depression and anxiety is to determine which disorder was the first to appear. For most patients with a mixed presentation, this is a helpful means of making sense of their complexity and enables a clear point of intervention.

There is little doubt, however, that some

IN SUMMARY

- **Comorbidity of depression and anxiety is generally associated with more severe illness.**
- **The most clinically useful approach to deciding on treatment for patients with mixed depression and anxiety is to determine which disorder was the first to appear.**
- **If the depression was the first condition to appear, or was subsequent but is marked or severe, treat the depression. Once the depression is adequately treated, address the anxiety disorder.**
- **If the anxiety disorder was the initial presentation and the depression is not severe, the first step should be treatment of the anxiety disorder.**
- **Treatment may involve pharmacological therapy, cognitive behavioural therapy (CBT), or both.**
- **It is a fallacy that depressed patients with anxiety symptoms necessarily require sedative antidepressants such as mirtazapine or the tricyclics.**
- **The two main cognitive vulnerabilities that put individuals at heightened risk of depression are interpersonal sensitivity and too much focus on achievement to feel worthwhile.**

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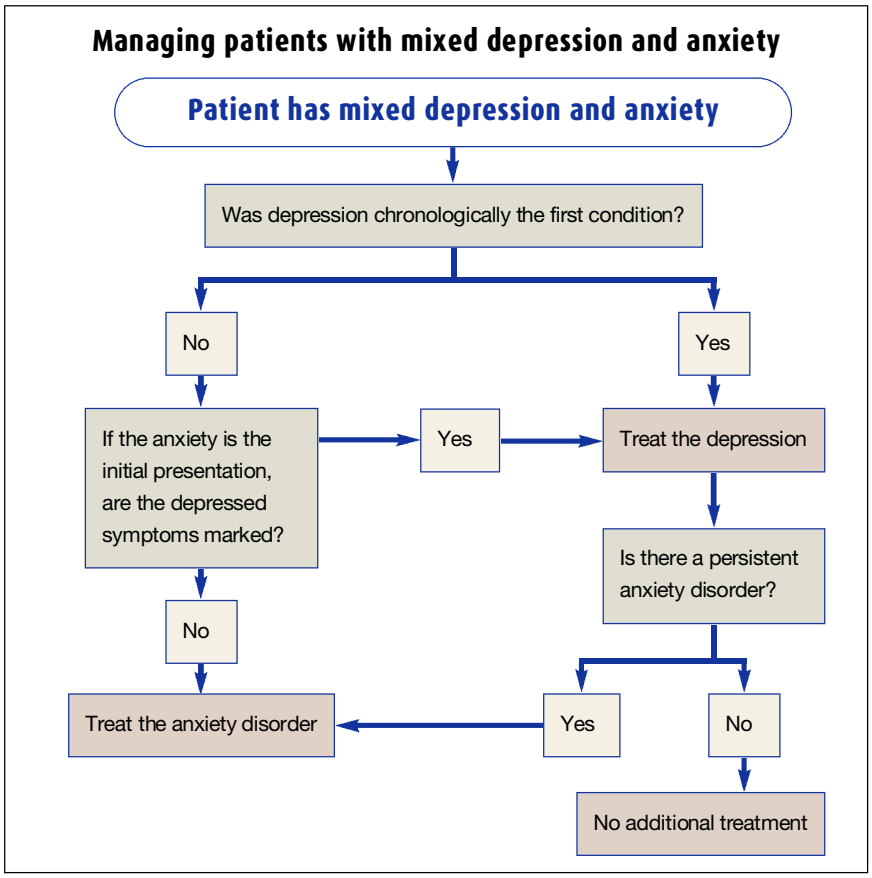

patients present with the concurrent onset of both depression and anxiety. For such patients the terms 'generalised distress syndrome' or 'generalised neurotic syndrome' have been applied. These terms are not recognised in the American DSM-IV or the WHO ICD-10 diagnostic classification systems. For patients who have anxiety and depression not sufficiently severe to fulfil the criteria for either a major depressive illness or a specific anxiety syndrome, the term 'mixed anxiety depression' has been coined. This controversial entity probably presents more commonly in general practice than in the psychiatric setting. At present, the diagnosis of 'mixed anxiety depression' has not been incorporated in the DSM system, though it is in the ICD-10 classification.

Clinically, anxiety symptoms may be the main manifestation of depression, and vice versa. It is therefore critical to enquire always about symptoms of both conditions. For example, anxiety presenting for the first time in an older patient may be indicative of an underlying depressive illness alone.

Principles of management

The principles of management are outlined in the flowchart above.

If the depression was the first condition to appear, the presentation should be treated as if it is a depressive illness. Furthermore, if the depression is clearly subsequent but is marked or severe then it should still be treated first. (Empirically it has been found difficult to treat anxiety disorders satisfactorily if there are significant levels of depression.) Once the depression is adequately treated then the anxiety disorder needs to be addressed in its own right.

If the anxiety disorder is the initial presentation and the depression is not severe, the first step should be treatment of the anxiety disorder. Usually the consequent symptoms or disorders resolve when the initial disorder is treated.

If the picture is one of 'mixed anxiety depression', the initial treatment is determined by the most severe symptoms (e.g. treat the depression first if that is most prominent).

Depression

For a diagnosis of major depression, at least five of the following symptoms must be present for at least two weeks (at least one of the first two symptoms must be included):

- depressed mood
- loss of interest or pleasure
- significant loss or gain of appetite or weight
- insomnia or hypersomnia
- psychomotor agitation or retardation
- fatigue or loss of energy
- feelings of worthlessness or excessive guilt
- impaired thinking or concentration, indecisiveness
- suicidal thoughts or thoughts of death.

Pharmacological therapy

As detailed guidelines on the use of antidepressant medications are available elsewhere (e.g. *Therapeutic Guidelines: Psychotropic*[3]), these will not be further discussed here. Some general comments on the treatment of depression with anxiety symptoms are, however, necessary.

First, although a small proportion of patients who are treated with antidepressants such as the selective serotonin reuptake inhibitors (SSRIs) or venlafaxine (Efexor-XR) develop anxiety as an adverse effect, the majority of patients experience a reduction of anxiety symptoms in parallel with the antidepressant response (see Case A on page 13). It is a fallacy that depressed patients with anxiety symptoms necessarily require sedative antidepressants such as mirtazapine (Avanza, Axit 30, Mirtazon, Remeron) or the tricyclics.

Second, despite claims to the contrary, there is no evidence that any particular antidepressant (such as a particular SSRI) is more effective than any other for treating depression with comorbid anxiety or panic. The only antidepressant that should perhaps be avoided in depressed patients with concurrent anxiety disorder is reboxetine (Edronax), which appears to produce relatively high rates of anxiety and insomnia.

CBT

CBT is based on the idea that depression is determined, at least in part, by the individual's negative thoughts, assumptions and underlying attitudes. Cognitions such as 'what's the point' or 'there is no hope for me' may serve to trigger and/or maintain depressed affect. Such negative thoughts generally prevent individuals from solving problems and regaining a sense of control.

There are two main cognitive vulnerabilities that make individuals at heightened risk of depression. The first is interpersonal sensitivity or the tendency to become excessively hurt by perceived or real rejection (for example, someone with this trait might notice that his or her partner is irritable on returning home from work, and take this personally despite reassurances to the contrary). The second is too much focus on achievement to feel worthwhile. Clearly, this places individuals at risk of depression if they are thwarted from achieving their goals, lose their job and so on.

The immediate goal of CBT is symptom relief through modifying negative thoughts. The longer term goal is to modify unhelpful underlying assumptions and solve problems in daily living or relationships, which in turn aims to prevent further episodes of depression.

Generalised anxiety disorder

The diagnostic criteria for generalised anxiety disorder include excessive anxiety and worry about a number of events or activities for a period of six months or longer. The anxiety and worry are associated with three or more of the following:

- restlessness or feeling 'keyed up' or on edge
- being easily fatigued
- difficulty concentrating or mind going blank
- irritability
- muscle tension
- sleep disturbance.

Case B, on this page, is a presentation of generalised anxiety disorder with secondary depression.

Pharmacological therapy

In general, pharmacological therapies play little role in the management of generalised anxiety disorder. Some antidepressants (such as venlafaxine and paroxetine) have received marketing approval for the treatment of this condition, but the clinical effect is modest.

Benzodiazepines are most useful for acute anxiety (up to one month) but become less effective with time. Daily use of benzodiazepines for more than one to two months is likely to lead to physical and/or psychological dependence.

Buspirone (Buspar) is a nonbenzodiazepine anxiolytic which does not induce dependence. Its effectiveness is, however, limited (and it is not PBS listed).

CBT

Individuals with generalised anxiety disorder are fearful and view themselves and situations around them as threatening. They are forever watchful for signs of danger and constantly anticipate that something bad is going to happen.

Negative cognitions revolve around

Case A. Depression with secondary anxiety

Mr E, a businessman in his early 60s, presented with anxiety and insomnia in the context of business difficulties. Although he had some perfectionistic traits and tended to be a worrier, he had never previously suffered from severe anxiety and had been very competent and successful in his career. On closer questioning, it was apparent that he was now reluctant to go to work, although he normally enjoyed this, thriving on the 'cut and thrust' of the commercial world. He had lost interest in his normal pleasures, such as golf and holidays. He had become forgetful and his concentration was impaired. He admitted feeling unhappy and depressed, although he had no suicidal thoughts.

Treatment with an SSRI antidepressant (coupled with counselling concerning his work situation) led to successful regulation of both his depressive and anxiety symptoms.

Case B. Generalised anxiety disorder with secondary depression

Mr K, a builder in his late 20s, presented with reactive depression in the context of stresses associated with his work. On further questioning, it became apparent that he had a long history of performance anxiety, perfectionism, obsessionality, fear of failure and hypersensitivity to criticism and rejection. He had experienced generalised anxiety and low self-esteem since adolescence and relied on praise from others to feel good about himself. When unable to deal with the stresses at work, he described feeling worthless, helpless and hopeless and had started abusing alcohol in an attempt to block out his emotions. Usually quiet and placid, he had become irritable and aggressive towards others.

He was treated with CBT focusing on the anxiety disorder.

Case C. Social phobia with secondary depression

Mr L was an overseas student in his early 20s who presented with depression consequent upon marked social phobia. Ever since his adolescence he had been markedly sensitive to being scrutinised by others. When he moved from overseas he became exquisitely sensitive to others looking at him, particularly in tutorials. As he continued in his studies he became less confident and began to become depressed and anxious. He found it difficult to concentrate, became hopeless about his future, and at times was preoccupied by suicidal thoughts.

After initial treatment with a series of antidepressants was unsuccessful, he received CBT, responding well to that.

Case D. Depression secondary to agoraphobia

Mrs S, a secretary in her late 40s, presented with agoraphobia with panic attacks and depression. She sought professional help after experiencing difficulty breathing when confronted with situations where escape routes were not readily available, the main problem areas being lifts, aeroplanes, tunnels, crowded places and public transport. She also expressed concerns about possible cardiac problems, fearing that she was going to die (all her medical investigations were normal). She had become frightened of leaving home and was unable to work.

She described being unhappy in her marriage and feeling trapped, describing her husband as domineering and unsupportive. Furthermore, her children had left home and were getting on with their own lives. She had lost interest in her usual activities and was becoming increasingly isolated, with feelings of inadequacy and hopelessness.

Her panic and depression responded well to CBT that was focused on the agoraphobia.

control, responsibility, predictability and safety. Individuals select out features in situations that confirm their perceptions of threat and danger. For example, someone with generalised anxiety disorder might not hear from a member of the family for a couple of days and become convinced that there is something wrong. CBT involves checking out the evidence for such beliefs and developing more realistic appraisal mechanisms.

Panic disorder

Panic disorder is recurrent panic attacks characterised by:

- palpitations
- sweating
- trembling
- dyspnoea
- choking sensation
- chest pain or discomfort
- nausea
- dizziness, light headedness
- derealisation
- fear of going crazy or dying
- tingling
- hot flushes.

Pharmacological therapy

All the SSRIs have been shown to be antipanic agents, and appear to be more acceptable than the tricyclics for this disorder. Alprazolam is also indicated for this condition, although withdrawal from this benzodiazepine is often difficult.

For illness not responding to other medications, the older monoamine oxidase inhibitors (MAOIs), such as phenelzine (Nardil) or tranylcypromine (Parnate), may be helpful. They do, however, have a higher risk of serious and even life threatening side effects.

CBT

Panic attacks result from the catastrophic interpretation of bodily sensations such as hyperventilation, palpitations, breathlessness and dizziness. Individuals with panic disorder become hypervigilant and perceive these sensations as signs of immediate physical or mental disaster leading to complete loss of control. For example, difficulty swallowing may be regarded as evidence of a choking attack; palpitations may be seen as indicative of a heart attack.

In this context, CBT involves using a combination of controlled breathing, progressive muscular relaxation, cognitive restructuring and exposure. It also involves identifying the sequence of events that trigger the panic attacks, which may include particular thoughts, images, bodily feelings or situations. The interpretation of these sensations is then examined and modified. Some individuals only believe that another interpretation applies if it can be shown in behavioural experiments, such as voluntary hyperventilation. Avoidance of particular situations may also reinforce negative interpretations, so CBT encourages individuals to approach situations that they may be been avoiding.

Social phobia and agoraphobia

Phobias are marked fears of situations or objects that are recognised by the sufferer as unreasonable or excessive and which interfere with normal function by the resulting discomfort or by measures taken to avoid the precipitating factors.

Social phobia is a marked and persistent fear of social or performance situations in which the person is exposed to unfamiliar people or to possible scrutiny by others (see Case C on this page). The individual fears that he or she will act in a way that will be humiliating or embarrassing.

Agoraphobia is the fear and avoidance

of being in places or situations from which escape might be difficult or embarrassing, or in which help might not be available in the event of suddenly developing a symptom that could be incapacitating or embarrassing (e.g. dizziness, derealisation, loss of bladder or bowel control). As a result of this fear, the person either restricts travel or needs a companion when away from home, or else endures agoraphobic situations despite intense anxiety (see Case D on page 14).

Pharmacological therapy

The major medications for social phobia are the SSRIs and the MAOIs – both the older agents (tranylcypromine and phenelzine) and moclobemide. In general, the clinical benefit from such medications is only moderate at best.

There are no specific medications for agoraphobia. All the treatments described for panic disorder can be used for agoraphobia associated with panic attacks.

CBT

The cognitive model views social phobia in terms of pervasive distressing thoughts related to the fear of being evaluated negatively or rejected. This generally leads to profound feelings of shame or embarrassment.

In addition to modifying beliefs, CBT involves graduated exposure to social situations that the individual has been avoiding because of high anxiety. Other techniques used to manage the anxiety include relaxation, distraction, role playing and rehearsal of typical situations. For maximum improvement, group CBT is recommended for people who have social phobia.

All the elements described for panic disorder may be applied to agoraphobia. The symptoms of agoraphobia generally centre on a marked avoidance of situations that individuals fear they will have difficulty escaping from. The fear of feeling anxious and subsequently being trapped is paramount. The further individuals with agoraphobia move away from their safe place, the more anxious they become.

CBT for agoraphobia will involve a combination of cognitive restructuring, graded exposure and behavioural experiments. Facing situations that are feared is fundamental to breaking the vicious cycle of anticipatory anxiety and avoidance. As with social phobia, group CBT is often beneficial.

Obsessive compulsive disorder

Obsessions are recurrent and persistent intrusive ideas, thoughts, impulses or images that are usually resisted by the patient and are recognised as the product of his or her own mind and not imposed from without.

Compulsions are repetitive, stereotyped behaviours in response to an obsession, to prevent discomfort or some dreaded event with which the rituals are not connected in a realistic way. The person generally recognises that his or her behaviour is excessive or unreasonable.

Pharmacological therapy

All of the SSRIs and the tricyclic clomipramine have been found to be effective for obsessive compulsive disorder. The anti-obsessive compulsive disorder effect is slower than the usual antidepressant action, with a delay of 8 to 12 weeks necessary before significant benefit is seen. Additionally, the dosage required to treat obsessive compulsive disorder is often higher than that required for depression – for example, 60 to 80 mg of fluoxetine may be necessary to obtain an anti-obsessional effect, unlike depression where 20 mg is usually sufficient.

CBT

Recurrent obsessive thoughts or images are generally distressing to patients. As a result, they may feel compelled to repeatedly perform certain compulsive rituals to neutralise the thoughts (e.g. excessive checking, ritualistic counting or hand washing).

Treatment involves deliberate and direct exposure to the feared thoughts and situations, and prevention (if relevant) of the compulsive behaviours and rituals. Therapy also includes habituation training, which involves getting individuals used to upsetting thoughts without their doing anything about them. Techniques include repeating the intrusive thoughts several times, writing them down repeatedly or using a tape-recorded loop of the thoughts in the individual's own voice. Another strategy involves 'thought stopping', which aims to consciously dismiss intrusive thoughts and so reduce their duration and intensity.

Conclusion

Comorbid depression and anxiety is common in clinical practice and leads to greater levels of disability. The principles of management outlined in this article should enable rational decision making about treatment choices, be they pharmacological, psychological or both. MT

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DECLARATION OF INTEREST: In the past three years, Professor Mitchell has served on an advisory board for Eli Lilly Australia and has received honoraria for lectures or consultations from AstraZeneca, Eli Lilly, GlaxoSmithKline and Janssen-Cilag. Dr Ball has received remuneration for advice to Eli Lilly.

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Assessing and managing social anxiety disorder

Of primary importance in assessing a patient with social anxiety disorder is judging the degree of functional impairment. Most patients with the condition will also have at least one comorbid psychiatric disorder, which should be assessed also.

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Social anxiety disorder is the extreme and persistent fear of social or performance situations, specifically the distress, anxiety and avoidance behaviours associated with the anticipatory belief that excruciating levels of embarrassment or humiliation will result from a social encounter. In the more severe cases, exposure to a particularly feared social situation (such as meeting strangers) may lead to a full-blown panic attack. Social anxiety disorder is also known as social phobia. Women are more likely to be affected than men, and the impact of the disorder on educational attainment and economic prospects can be severe.

Like depression, social anxiety disorder has a high prevalence rate – several large community studies claim that between 7.3 and 13.3% of the population will suffer from it at some time in their lives.[1,2] Estimates of lifetime prevalence are lower (around 2%) if social anxiety disorder with a greater degree of impairment and fears generalised to many situations is considered.[3] A specific fear of public speaking, for instance, is common in the general population, but may not significantly impair a person's overall functioning. By contrast, the fear of interacting with others is much more incapacitating. Typical situations that evoke fear in patients with social anxiety disorders are listed in Table 1.

Symptoms

Patients with social phobia may have symptoms ranging from excessive shyness to overwhelming and disabling panic associated with a particular situation. There are two broad types of social anxiety

IN SUMMARY

- **Social anxiety disorder, or social phobia, is an incapacitating fear of social or performance situations.**
- **Symptoms range from excessive shyness to overwhelming and disabling panic.**
- **Most patients with social anxiety disorder will have at least one comorbid psychiatric disorder, such as major depression, another anxiety disorder, avoidant personality disorder, or substance use disorder.**
- **Generalised social anxiety disorder is the more potentially disabling form and is typically chronic and unrelenting, extending to all aspects of a patient's social interactions and often associated with a family history. Comorbid disorders are more common.**
- **Nongeneralised social anxiety disorder is an excessive fear of one or a limited number or kinds of social situation, such as public speaking or eating in public.**
- **Causes of social phobia are multifactorial and thought to include prior experiences, negative thinking, genetic predisposition and, for some, a paucity of social skills.**
- **Current recommended treatment options include cognitive behavioural therapy and pharmacotherapy. Antidepressants are the first line pharmacotherapy; anxiolytics may sometimes be useful as short term or adjunctive measures.**

Table 1. Feared situations for patients with social anxiety disorder

- Speaking in public
- Taking tests and being examined
- Eating, drinking and writing in the presence of others
- Performing work duties under observation
- Using public toilets in the presence of others
- Interactive situations where there is an expectation to communicate with others

Table 2. Symptoms reported in social anxiety disorder

Physical symptoms

- Breathlessness or rapid, shallow breathing
- Sweating
- Shakiness/trembling
- Nausea or 'butterflies'
- Heart palpitations
- Dizziness

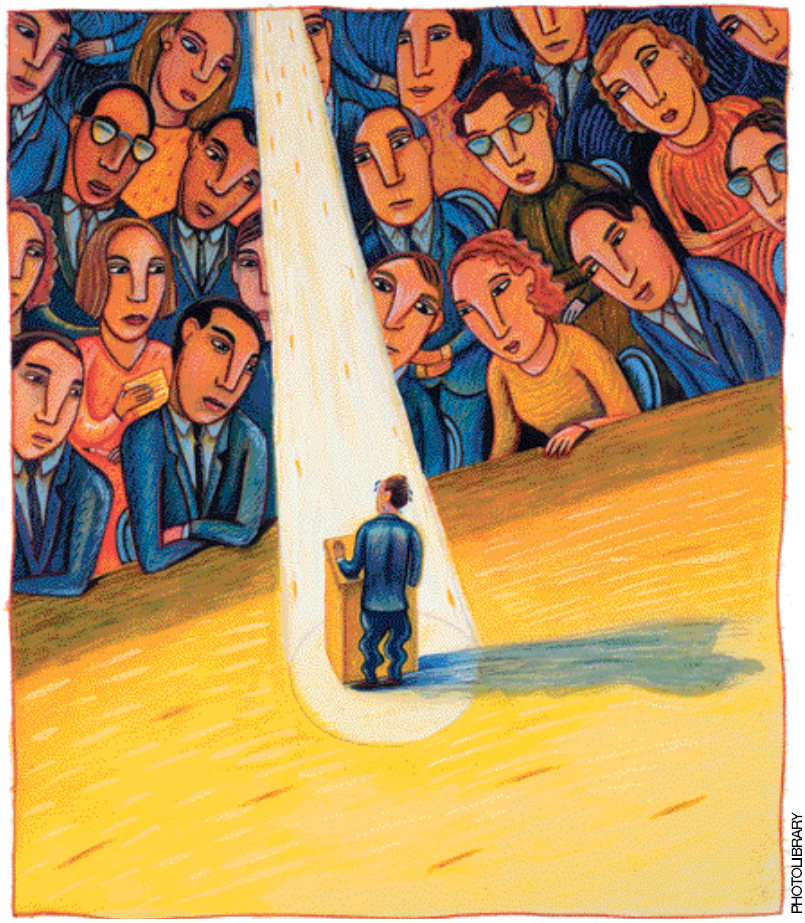
Behavioural symptoms

- Flight
- Avoidance
- Freezing

Cognitive/emotional symptoms

- Fear of evaluation, such as 'people will think I'm stupid/unattractive/incompetent'
- Emotions such as shame, embarrassment, anger or fear

disorder: generalised and nongeneralised. Generalised social anxiety disorder often develops in childhood or adolescence, and is the more potentially disabling form of the condition. It is typically chronic and unrelenting, extending to all aspects of a patient's social interactions, and is often associated with a family history and with comorbid disorders. Nongeneralised social anxiety disorder is an excessive fear of one social situation in particular or of a limited number or kinds of situation, such as eating in public. A genetic link seems to be stronger for generalised social anxiety disorder.



PHOTOLIBRARY

In both types of social anxiety disorder, patients are likely to harbour irrational beliefs about themselves (for example, 'they don't like me' or 'I'm not interesting) and about their anticipated performance in social situations (for example, 'everyone will see my hand trembling and it will be a disaster'). There are usually involuntary physical symptoms associated with the anxiety, such as shaking or sweating, as well as behavioural symptoms, often manifested by a complete incapacitation during, or total avoidance of, the feared social situation. Table 2 lists some of the symptoms that patients with social phobia report when anticipating or facing a feared social situation.

If a panic attack occurs, the physical symptoms listed above are severe and there may be others as well, such as numbness or flushing. Additional cognitive symptoms are also often described, such as feeling 'unreal' or detached, commonly reaching a peak within 10 minutes. Thoughts may be compounded by fears of losing control or of dying.

Diagnosing social anxiety disorder

Summary of DSM-IV diagnostic criteria for 300.23 social anxiety disorder (social phobia)[4]

A. A marked and persistent fear of one or more social or performance situations. The individual fears that he or she will act in a way that will be embarrassing.

B. Exposure to the feared social situation almost invariably provokes anxiety.

C. The person recognises that the fear is excessive or unreasonable.

D. The feared social or performance situations are avoided.

E. Significantly interferes with the person's normal routine, occupational (academic) functioning, or social activities or relationships.

F. In individuals under age 18 years, the duration is at least six months.

Differential diagnoses

Social anxiety disorder often coexists with panic disorder. DSM-IV lists the differential diagnoses of social anxiety disorder as Panic Disorder with Agoraphobia and Agoraphobia without History of Panic Disorder. Social anxiety disorder also shares many features with avoidant personality disorder, which should be considered as an additional diagnosis. The distinction between social phobia and avoidant personality disorder is that social phobia is essentially a problem of performing in social situations, whereas the avoidant personality has a problem relating to other people.

Assessment

Taking a careful and complete psychiatric history as well as performing a thorough medical assessment in a patient who may have social phobia will enable an accurate diagnosis (see the box on this page).[4] Of primary importance is judging the degree to which the patient is disabled and/or functionally impaired by the anxiety. The severity of avoidance behaviours should also be established.

Most patients with social phobia will have at least one, and frequently more, comorbid disorders, and it is vital to assess these. Where the patient's social anxiety is of the generalised type, comorbid psychiatric conditions are even more likely. The association between social phobia and major depression is particularly strong; up to 37% of patients with social anxiety disorder have a diagnosis overlap with major depression.[3] Although diagnostic features are discrete, it may be that the frequent presence of low self-esteem ensures many patients have both diagnoses.

Often social anxiety coexists with other anxiety disorders as well as avoidant personality disorders. Comorbidity rates may be as high as 30 to 40% for simple phobia and social anxiety disorder. Similarly, 14% of patients with social anxiety disorder may have substance use disorders. The relationship between diagnoses is complex: for instance, the secondary use of alcohol to relieve social anxiety may lead to substance misuse. Clinical treatment therefore needs to take into account any comorbidities that may exist. Most treatments described for social anxiety disorder in this article also have benefits for depression and other anxiety disorders.

There are several rating scales that can be useful in screening for social anxiety disorder, such as the Mini-SPIN, the Brief Social Phobia Scale and the Social Phobia Inventory (SPIN).[5-7]

Social phobia is underdiagnosed. It is important to explore patient reports of avoidance of social interactions and to challenge patients who accept this as a way of life.

Causes of social anxiety disorder

Causes of social anxiety disorder are multifactorial and thought to include prior experiences, negative thinking, genetic predisposition and, for some, a paucity of social skills.

Prior experiences (conditioning models)

Traumatic or embarrassing social interactions in the past may have caused an individual to have an anxious response each time, characterised by humiliation, embarrassment or rejection. This may become a conditioned response that is then elicited in similar situations. Avoidance serves to maintain social phobias because avoidance of feared social situations decreases anxiety, thereby powerfully reinforcing the avoidance.

Negative thinking (cognitive model)

There is considerable research support for the role of cognitive factors in social anxiety disorder. Two themes commonly found in cognitive analysis of patients with social phobia are the anticipation that one will be evaluated negatively and fears of performance failure. This cognitive process is likely to be directly involved in the onset and maintenance of the condition. The 'social phobic' is often hypersensitive to signals from other people regarding personal acceptability (behaviour or appearance) and this interacts with a negative self-view, resulting in anxiety, which may impair performance and activate fears of failed performance.

Genetic predisposition

There is substantial evidence for the existence of family liability for social anxiety disorder. Relatives of patients with social phobia have been found to have a significant increased risk of social anxiety disorder but not of other anxiety disorders, although this may only be so for

the generalised type. What is inherited, however, may be a trait that predisposes individuals to social anxiety disorder. 'Behavioural inhibition' is a temperamental trait described in children who are wary of novel stimuli and may withdraw from unfamiliar objects or people. Behavioural inhibition increases risk of social phobia. While inherited traits may predispose a child to the condition, early life experiences and parental modelling no doubt modulate genetic predisposition.

Poor social skills (skill deficit model)

Controversy exists within the literature as to whether those individuals with social anxiety truly lack social skills or whether their anxiety inhibits the use of existing skills.

Treatment options

Current recommended treatment options for social anxiety disorder include cognitive behavioural therapy (CBT) and pharmacotherapy.

Psychological treatments

The use of CBT has gained increasing support. The advantages of cognitive behavioural programs include their efficacy in preventing relapse. Treatment can be delivered individually or in groups, the latter having the advantage of exposing the client to the feared situation and receiving direct feedback from others.

With the advent of Medicare funding involving psychologists, psychological treatment may become more routinely used in general practice. This will necessitate good relationships with GPs and basic knowledge of psychopharmacology.

Typical psychological treatment programs involve the components discussed below.

Basic information and self-monitoring

Informing patients about the symptoms and causes of social anxiety disorder is useful, as is teaching them how to develop behavioural skills such as self-monitoring of behaviour in feared situations. This forms the basis for understanding triggers and recognising progress when it occurs.

Cognitive therapy

Cognitive therapy based on the work of Beck and colleagues is a central component of treatment and aims to alter exaggerated thoughts and beliefs.[8] Patients with social anxiety disorder have beliefs that others will view them negatively, including judgements of incompetence and high expectations of performance.[9] Incorrect interpretation of a situation results in irrational beliefs, which then have a major influence on subsequent emotions and behaviour. Treatment involves the two steps listed below:

- Monitoring and identifying thoughts and beliefs. For example, a patient may report unhelpful thoughts such as 'I will look stupid because I don't know how to ask to buy tickets correctly'. Helping patients learn to identify these thoughts and record them is a first step to treatment.
- Introducing more rational thoughts. This is achieved by challenging the probability and consequence of negative outcomes. It is helpful for challenging statements to be developed, such as 'There is no "correct" way of asking for tickets. Even if I ask in a way that is unusual, I will still get the tickets. If I worry too much about how I look to others, I may not get things done'. Patients are encouraged to use such positive self-statements and perhaps reward themselves for developing challenging thoughts.

Refocusing attention

Patients are encouraged to refocus attention away from negative thoughts to the task at hand.

Actual exposure

Actual exposure to feared social and performance situations addresses avoidance behaviour and achieves anxiety reduction by habituation. Exposure also reinforces the message that negative evaluation, even if it occurs, is not as terrible as anticipated. This treatment component involves setting goals and timetables for exposure and developing an exposure hierarchy. Ideally exposure should be graduated, repeated and prolonged. However, given the unpredictability of social situations, caution needs to be exercised. An example of exposure for a patient concerned with what people think is the trying on of four coats and the buying of none of them.

Improving social performance

Social performance can be improved by providing feedback and teaching social skills. This is only relevant for patients who are truly lacking in social skills because for most patients the problem is more negative self-evaluation of performance rather than a skill deficit. Nevertheless, for some it can be helpful to teach strategies to improve nonverbal communications (such as increased eye contact, an 'open' attitude and sufficient volume of voice) and verbal skills (such as active listening, communication of feelings, and the giving and receiving of criticism).

Relaxation techniques

Relaxation techniques are often used to reduce anxiety. Patients are taught behaviours that counteract the physical effects of anxiety (for example, exercises that aim to release tension in muscles) as well as the use of psychic techniques to reduce anxiety (for example, the use of pleasant imagery).

Pharmacotherapy

Medication in the management of anxiety may be an important part of treatment. The decision to use medication should be determined on an individual basis, and risk–benefit considerations vary with the disability caused by the symptoms and the age of the patient, as well as other factors.

Table 3. Pharmacotherapy for social anxiety disorder*

First line drugs

Antidepressants

- SSRIs
  - escitalopram (Lexapro)
  - paroxetine (Aropax, Oxetine, Paxtine)
  - sertraline (Concorz, Eleva, Xydep, Zoloft)
- Tetracyclics
  - mianserin (Lumin, Tolvon)
  - mirtazapine (Avanza, Axit 30, Mirtazon, Remeron)
- SNRI – venlafaxine (Efexor)
- NARI – reboxetine (Edronax)
- Tricyclics (occasionally)
- MAOIs

Other drugs

Anxiolytics (for short term use only)

- Alprazolam (Alprax, Kalma, Xanax, Zamhexal)
- Diazepam (Antenex, Ducene, Valium, Valpam)
- Lorazepam (Ativan)
- Oxazepam (Alepram, Murelax, Serepax)

Beta blockers

Evidence for efficacy is controversial

* Not a comprehensive list

Many drugs may be used in the treatment of social anxiety disorder (Table 3), the choice depending on the severity and the symptom complex, and also the physician or psychiatrist's personal experience. Patients taking medications for social anxiety disorder should be reviewed regularly, and some do better if they are on medication for a longer period.

Antidepressants

Antidepressants are the first line treatment and have been shown to be effective in the management of social anxiety disorder. Several classes of antidepressants are used:

- selective serotonin reuptake inhibitors (SSRIs) – sertraline, escitalopram and paroxetine; used most commonly
- tetracyclics – mianserin and mirtazapine
- serotonin and noradrenaline reuptake inhibitors (SNRIs) – venlafaxine
- noradrenaline reuptake inhibitors (NARIs) – reboxetine
- tricyclics; used only occasionally
- monoamine oxidase inhibitors (MAOIs).

The most commonly used antidepressants, the SSRIs, are generally well tolerated, have a benign side effect profile, are safe in overdose and are effective against frequently occurring comorbid conditions such as depression.[10] These newer antidepressants are generally preferred over nonselective irreversible MAOIs such as phenelzine (Nardil) because of the latter's serious interaction with foods high in tyramine.

It is important to inform patients that taking antidepressants is not a sign of weakness and that these drugs are not addictive. Patients should also be aware that antidepressants need to be taken regularly and that it will be two to three weeks before they have any effect and up to six to eight weeks before they are having their full effect. It is usual to start on a low dose and then slowly increase the dose, depending on the effects and the patient's response. It is also important to remember that antidepressants interact with other medications, including herbal medicines such as St John's wort.

Anxiolytics

Anxiolytics, classically benzodiazepines, as a class are not a first line treatment for patients with social anxiety disorder because the condition requires long term treatment and dependence problems may arise. Furthermore, comorbid conditions such as depression or alcohol misuse are not effectively treated by anxiolytics.

Nevertheless, at times benzodiazepines may be considered useful as a short term or adjunctive measure and have shown efficacy with social anxiety disorder. Most benzodiazepines are relatively nontoxic in overdose, but there are differences between drugs (depending on their absorption rates and sedation effects). There are RACGP guidelines for the clinical use of benzodiazepines,[11] and the most frequently used include alprazolam, diazepam, lorazepam and oxazepam. Pharmacological properties of these drugs are essentially similar. When patients are prescribed anxiolytics, short term evaluation and/or intermittent courses should be considered.

Other drugs

Apart from anxiolytics and antidepressants, beta blockers have also been used to treat social anxiety disorder, although evidence for their efficacy is more controversial.

What the GP can do in the management of social phobia

Assessment

The GP plays an important role in the assessment of patients with social anxiety disorder, being well placed to take the history and diagnose the presence of the condition (generalised or nongeneralised) and comorbid conditions such as depression. Some GPs may find that the use of rating scales assists them with their diagnosis and can be easily incorporated into general practice.

General practice management

For nongeneralised social anxiety disorder, referral to a specialist may not always be needed, and the principles outlined in this article can form the basis of a supportive approach. Simple anxiety management and positive thinking techniques can help, for example:

- help the patient to identify negative thoughts in social situations and then challenge them

- help the patient to develop relaxation techniques that can be applied before a feared performance or social situation.

Medication may be required when the condition is more severe and not responding to other approaches.

Referral

For severe and generalised social anxiety disorders a shared care arrangement is best. The GP is in an ideal position to monitor the progress of therapy and decide whether onward referral to a psychiatrist or psychologist is needed. In general, if progress is not occurring or the condition is severe then referral is appropriate. Referral to a psychologist is particularly helpful for in-depth work with psychological issues that may have emerged and for challenging entrenched negative thinking. The following questions should be kept in mind:

- is there a need for follow up?
- how will the patient's progress and the efficacy of therapy be monitored?
- what alternative therapy might be tried if the current therapy is unsuccessful?

Prognosis

Factors suggesting a poor prognosis include social anxiety disorder of a complex generalised subtype, very early onset (before age 7 to 11 years), greater initial severity, greater number of symptoms, co-occurring psychiatric disorders, presence of depression, presence of health problems and lower education.

Patients with social phobia can be slow to show a response to therapy. Those whose symptoms improve to the point of recovery tend to stay well.

Conclusion

While social phobia has a high lifetime prevalence (up to 13% suffer from it at some point in their lives), it is treatable using several pharmacological and psychological approaches. The GP can play a central role in assessing patients and deciding when simple management techniques and/or pharmacotherapy can help and when specialist help is needed. MT

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DECLARATION OF INTEREST: None.

Generalised anxiety disorder
focus on adults

Most patients with generalised anxiety disorder can be treated by GPs. Psychological techniques such as cognitive behavioural therapy and pharmacotherapy with the newer antidepressants form the basis of treatment.

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Generalised anxiety disorder is common but has not been the focus of attention and therapeutic endeavour to the same degree as other anxiety disorders or depressive illness. It is disabling and recurrent, and frequently comorbid with other anxiety and depressive illnesses and also with alcohol abuse.

Generalised anxiety disorder has, until recently, been ignored for several reasons. There was uncertainty from earlier research as to whether it was a separate disorder or was always linked with other anxiety disorders or depression. *In the Diagnostic and Statistical Manual of Mental Disorders (DSM)-III's* hierarchy of diagnoses, which ranged from organic disorders to psychoses, generalised anxiety disorder was almost a residual category.[1] Although the hierarchy has generally been removed in *DSM-IV*, the tendency persists to ignore generalised anxiety disorder in the presence of, for example, depressive illness.[2] In contrast to the lack of emphasis on this disorder in the medical arena, the lack of focus on the disability from it and the need for effective treatment, it is well recognised in the general community and in literature.

Anxiety is not always disabling. It can have a quality of helping alertness, focus, motivation and concentration, as can be seen in improved performance in examinations. It is only when the anxiety gets out of control that performance may decrease and disability ensue. Such a reaction with disability persisting for more than six months could represent generalised anxiety disorder.

Some people by nature have an anxious temperament. This is to say that they are characteristically more anxious than most people. This anxious temperament is not disabling in the way that a person can be disabled with generalised anxiety disorder. These people can, like anyone else, be disabled with generalised anxiety disorder if they get more anxious. When assessing anxious patients,

IN SUMMARY

- **Generalised anxiety disorder is a recurrent and disabling condition that affects up to 6% of the population at any one time. Women are affected more than men.**
- **GPs can treat almost all patients with generalised anxiety disorder.**
- **Cognitive behavioural therapy can be helpful on its own, especially if symptoms are mild.**
- **Pharmacotherapy, particularly with the newer antidepressants, is first line treatment, both in the acute phase and for long term maintenance.**
- **Benzodiazepines have little role in treating patients who have generalised anxiety disorder. They may be useful in exacerbations but should not normally be continued beyond the acute phase.**

the persistence of the anxiety and the degree of disability it is causing should be determined as well as whether an anxiety state is present.

Definitions

The diagnostic criteria for generalised anxiety disorder include:[2]

- excessive anxiety and worry, occurring more days than not for at least six months, about a number of events or activities (such as work or school performance)
- the person finds it difficult to control the worry
- the anxiety and worry are associated with three or more of the following symptoms:
  - restlessness or feeling keyed up or on edge
  - being easily fatigued
  - difficulty concentrating or mind going blank
  - irritability
  - muscle tension
  - sleep disturbance (difficulty falling or staying asleep, or restless unsatisfying sleep).

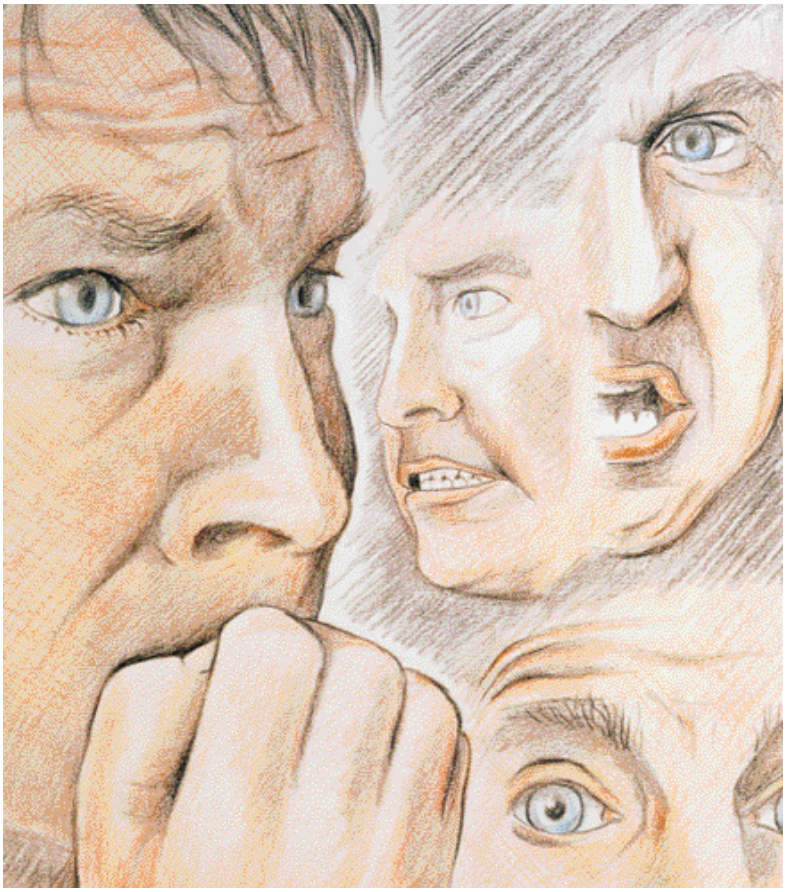
The more persisting enduring anxiety of generalised anxiety disorder is different from the episodic anxiety of panic disorder, the obsessive ruminations and compulsive behaviour of obsessive compulsive disorder and the avoidance behaviour seen with agoraphobia or social anxiety disorder (social phobia).

Epidemiology

Rates of generalised anxiety disorder of between 2.8 and 8.5% have been reported, with a median prevalence of 5.8%.[3] The condition commonly occurs together with mood and personality disorders and has an increased incidence of associated alcohol abuse. Coexisting personality disorder can occur in 60% of patients who have generalised anxiety disorder.[4] Generalised anxiety disorder affects women more frequently than men, with a 10% prevalence in women aged over 35 years.[5] Patients with generalised anxiety disorder demonstrate a degree of impairment similar to that seen in patients with major depression.[5]

It has been suggested that there is a pathway towards generalised anxiety disorder from having an anxious temperament. This is a preliminary aetiological model that needs further research.[6]

The diagnostic validity of generalised anxiety disorder has been questioned. Because of the frequency with which other anxiety and depressive disorders are comorbid with generalised anxiety disorder, it has been concluded that the construct validity of generalised anxiety disorder was inconsistent.[7] However, it has been recognised recently that this comorbidity is no more common with generalised anxiety disorder than with the other anxiety and depressive illnesses. This challenge to the diagnostic validity of the disorder may, therefore, not be as important as previously considered.[8]



PHOTOLIBRARY

Predictors of recovery

The outcome of generalised anxiety disorder depends on its comorbidity. It has been shown that patients with simultaneous anxiety and depressive diagnoses have a worse outcome compared with those with a single anxiety or depression diagnosis and with low depression scores.[9] In contrast, those who achieve significant improvement in symptoms in the first 10 weeks of treatment maintain that improvement after five and 12 years. Importantly, patients with generalised anxiety disorder and another diagnosis incur greater health costs over 12 years than those with single diagnoses.

Patients meeting all the criteria for generalised

anxiety disorder have been shown to have a worse outcome than those meeting all the criteria other than excessive worry.[10] Those with excessive worry had an illness that began earlier in life, had a more chronic course and was associated with greater symptom severity and psychiatric disability than nonexcessive generalised anxiety disorder.

Well over half of primary care patients with generalised anxiety disorder have been shown to continue to experience significant symptoms of the disorder after two years of prospective follow up.[11] A substantial proportion of those who experienced a period of full recovery had a recurrence of symptoms just within the two-year period of observation. Diagnostic comorbidity, severity of psychosocial impairment and female sex were all associated with a lack of recovery. These findings add to mounting evidence that generalised anxiety disorder is a chronic and recurrent anxiety disorder.[12,13]

Evidence based psychological treatments

Psychological treatments for generalised anxiety disorder with a sound evidence base include cognitive behavioural therapy (CBT), acceptance and mindfulness, brief psychodynamic therapy and wellbeing therapy.

CBT

CBT is suitable for use in general practice. The basic processes involve educating patients and teaching them basic skills for controlling their anxiety (that is, relaxation and breathing control). In addition, patients can be taught to identify, challenge and change maladaptive thoughts, feelings, perceptions and behaviours (see the box on this page).[14] Treatment typically involves 12 to 25 sessions of treatment and may well involve some later booster sessions.

There have been several recent reviews of CBT.[15-17] It can be efficacious, but substantial limitations are documented in the research literature. It has been shown to be effective but the results of comparisons between it and pharmacotherapy vary according to the meta-analytic methods used, therefore limiting the use of such comparisons. When only studies that directly compared CBT and pharmacotherapy were included in the analysis, there were no significant differences in efficacy.

Even elderly patients (those aged over 65 years) with generalised anxiety disorder can show improvement with CBT. It has been reported that about half of older adults with the condition show a significant improvement at the end of treatment, and two-thirds show this six months later.[18]

CBT for generalised anxiety disorder

- Educate the patient about generalised anxiety disorder
- Explain that physical symptoms such as muscle tension are a consequence of the anxiety and not automatically an indicator of some serious physical illness
- Teach the patient skills for anxiety control – relaxation and breathing (hyperventilation) control
- Teach the patient to identify, challenge and change maladaptive thoughts, feelings, perceptions and behaviour
- Teach monitoring techniques and consider the use of patient charts to monitor and help change thoughts, feelings and behaviours[14]*

* Patient charts and more detailed discussion of CBT are given in reference 14, the full text of which is available free online (www.australianprescriber.com/magazine/24/2/33/7).

There remains a common assumption that CBT will always work. This treatment is significantly less effective for severely affected patients, and trials that compared CBT with a wait-list control found significantly larger effect sizes than those comparing CBT to an attention placebo, but not to a pill placebo.[19] This is clinically useful as it suggests pharmacotherapy, either alone or possibly in conjunction with CBT, might be more effective in patients with severe illness.

Other psychological treatments

Acceptance and mindfulness

When there is anxiety that is resistant to treatment and a desire to use psychologically based treatments, acceptance and mindfulness are helpful approaches that can be added to CBT.[20] Instead of trying to change difficult thoughts and feelings as a means of coping, acceptance and mindfulness based therapy helps patients learn to tolerate difficult emotions and overcome depressing thoughts by observing their thoughts, emotions and bodily sensations in a nonjudgemental manner.

Psychodynamic therapy

Brief psychodynamic therapy (in which the bringing of the unconscious into conscious awareness promotes insight and resolves conflict) was a mainstay in treating anxiety disorders but has fallen out of favour in comparison with what are generally regarded as more effective CBT-based treatments. There can be positive outcomes from this therapeutic approach, although the outcomes are worse if there are a comorbid major depression, interpersonal issues or negative expectations.

Longer term psychodynamic therapy can be considered as an alternative psychoanalytically orientated approach that might improve treatment success rates in generalised anxiety disorder.[21]

Wellbeing therapy

Another adjunctive approach is the use of 'wellbeing therapy'. In this therapy,

patients are asked to report only episodes of wellbeing in a diary. Automatic thoughts leading to premature interruption of wellbeing are identified and specific impairments become the focus of attention. Furthermore, mastery and pleasure tasks are used in addition to exposure to feared situations. This approach has been shown to provide better outcomes than CBT alone.[22]

Evidence based pharmacotherapy

Pharmacotherapy has been shown to be superior to placebo in treating generalised anxiety disorder in a large number of controlled studies, and efficacy is suggested from open studies as well. Evidence is available for benzodiazepines, azapirones, venlafaxine, sertraline, escitalopram, paroxetine and mirtazapine.[23-27]

Antidepressant agents are preferred nowadays over the use of benzodiazepines or other tranquillisers.

Tranquillisers

The traditional mainstays of antianxiety therapy have been the barbiturates and then the benzodiazepines. In the community at large, alcohol is commonly used for similar effects. Although these agents can produce quite rapid reduction of symptoms, the reduction may not be sustained. Other problems with these agents are the gradual development of tolerance (with patients progressively increasing their dose), dependency and, on discontinuation, withdrawal symptoms. Also, older patients taking benzodiazepines are more likely to experience falls.

The major tranquillisers (typical antipsychotics, sometimes referred to as first generation antipsychotics) can also provide some acute relief. These have added complications in that a proportion of patients will show acute extrapyramidal side effects and an increasing proportion will, with continued use, suffer from the potentially permanent neurological movement disorder of tardive dyskinesia.

The various problems with these agents have brought about a major change in the pharmacotherapy of generalised anxiety disorder, and tranquillisers are now relegated to a secondary role, more commonly being used for the brief treatment of exacerbations rather than as continuing therapy.

Azapirones

Buspirone (Buspar) is the only agent available in Australia of the class of non-benzodiazepine anxiolytic agents known as the azapirones. It can be a useful agent for some patients who are troubled with long term generalised anxiety but tends to be of lower effectiveness if prescribed following the use of benzodiazepines.

Buspirone takes up to four weeks to build up to effectiveness but does not have problems of tolerance and dependency. However, its use in Australia is limited by cost as it is not listed on the PBS.

Antidepressants

Antidepressants are now the mainstay of pharmacotherapy of generalised anxiety disorder. These agents are misnamed as they are useful agents for a broad spectrum of anxiety disorders, yet may be unhelpful for some patients with certain types of depression, such as bipolar depression.

The first line agents for generalised anxiety disorder are the selective serotonin reuptake inhibitors (SSRIs) and the serotonin and noradrenaline reuptake inhibitor (SNRI) venlafaxine (Efexor). These agents are efficacious for many patients suffering from anxiety and depression and are well tolerated.[27] They should be started at a low dose to minimise initial anxiety, and the dose then increased to therapeutic levels as soon as tolerated.

Agents approved by the TGA in Australia for use in generalised anxiety disorder are escitalopram (Lexapro), paroxetine (Aropax, Oxetine, Paxtine) and venlafaxine. In practice, it is likely that any of the SSRIs, SNRIs or other modern antidepressants are likely to be effective for generalised anxiety disorder, both for acute therapy and for long term maintenance.

Other possible pharmacotherapy

Other agents are being studied for the treatment of generalised anxiety disorder but none of these are available in Australia. It is expected that newer treatments will become available in the next few years.

Long term therapy

It would be expected that long term treatment would become the norm as generalised anxiety disorder is recurrent. Unfortunately, most pharmacotherapy studies do not extend beyond the acute phase of six to eight weeks. Studies of paroxetine and venlafaxine have shown both short term efficacy and maintenance of long term remissions as well as restoring good social functioning.[28]

The GP's role

The GP has a central role in identifying and treating generalised anxiety disorder. It should first be established whether the patient has generalised anxiety alone or in conjunction with some other anxiety or depressive disorder. The degree of disability from the anxiety and whether it is of shorter duration or longstanding should also be determined. Few patients need referral to specialists, although some GPs may prefer to refer for treatment.

An initial CBT approach will be effective for many patients, and can be undertaken by a GP, psychiatrist or psychologist. This psychological approach can be enhanced by other talking techniques.

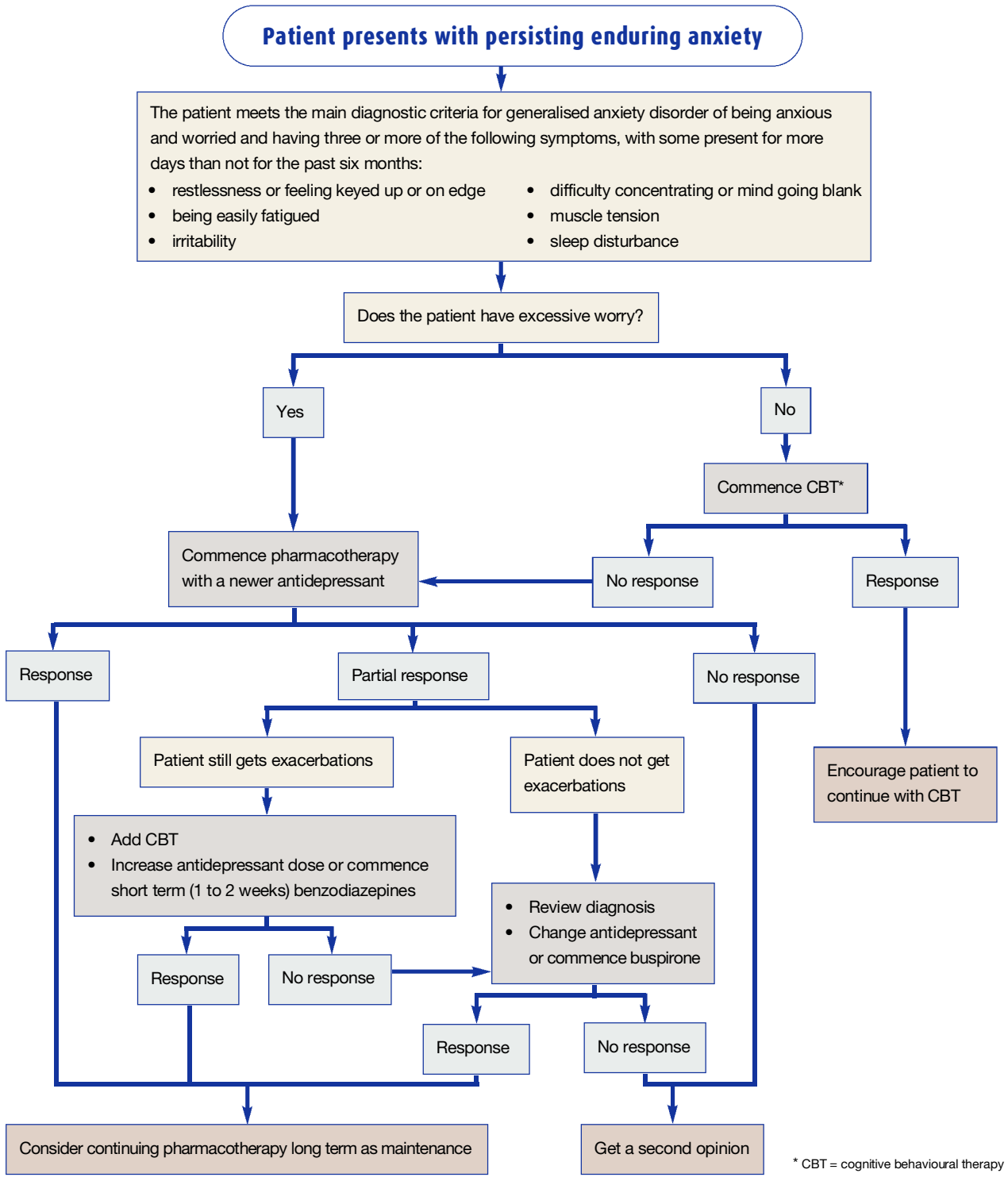
If acute symptomatic relief alone is sought, a benzodiazepine may be considered. However, the prescriber should be mindful of the potential to generate long term use and dependency following initial short term intent.

For acute therapy, longstanding anxiety or if anxiety does not settle, pharmacotherapy with an SSRI or venlafaxine should be considered. Buspirone remains an alternative agent for those who can afford it.

The aim of therapy should not just be

continued

An approach to managing generalised anxiety disorder



symptom reduction, but also a return to normal psychosocial functioning.

Conclusions

Generalised anxiety disorder is a common, recurrent and persisting disorder. It is disabling, and is frequently associated with another anxiety or depressive disorder, or with substance abuse such as of alcohol.

An initial approach using CBT may be sufficient if symptomatology is not too severe. Otherwise, pharmacotherapy with one of the newer antidepressant agents is the first line acute and long term treatment. The combination of pharmacotherapy and CBT may provide better outcomes for some patients. Management is summarised in the flowchart on page 26.

Although benzodiazepines can be useful for acute symptomatic relief, the risks of tolerance and dependency outweigh the benefits of their use for most patients. Several newer drugs are being explored as therapeutic options for this disorder. MT

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DECLARATION OF INTEREST: Professor Tiller has been a member of advisory boards and has undertaken consultancies in respect of almost all antidepressants and tranquillisers. He is currently undertaking industy supported studies on such agents.

Diagnosing and managing depression in adults

The profound effect that even mild depression can have on the quality of life of an individual and his or her family should not be underestimated. The condition is often not recognised when patients present with it, and patients in whom it is diagnosed are often undertreated.

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Depression is a common and treatable disorder with a 12-month prevalence of 7.4% for women and 4.2% for men.[1] While the highest prevalence rates are among young adults, it is important to remember that the young, especially teenagers, and the elderly are also liable to develop depression. Depression carries with it a high disease burden; it has been estimated that by the year 2020 depression will be the second most burdensome disease worldwide.

Although depression is common and treatable it often goes unrecognised and untreated. In a recent national mental health survey, over half of those people with depression had not sought treatment for their depression.[2] Up to half of those that presented for treatment did not have their depression recognised, and undertreatment was common among those whose depression was diagnosed. Most of those who did seek treatment went to GPs; hence, depression accounts for a large number of presentations in primary care.

Management principles

The successful management of depression requires:

- recognition of clinical depression when it presents
- clarification of the type and severity of depression
- suicide risk assessment
- identification of antecedent, precipitating and maintaining psychosocial factors
- psychoeducation
- implementation of specific treatment strategies based on patient preference and the evidence base.

Diagnosis

A diagnosis of depression is straightforward when the patient complains of depressive symptoms. The key issue here is to determine whether such symptoms are an extreme of 'normal' depression or pathological. Depression is a normal human emotion; all of us can experience a depressed

IN SUMMARY

- **Management of depression includes the correct identification of clinical depression, distinguishing pathological from 'normal' depression, assessment of risk to self and to others, psychoeducation of the patient and patient's family, and application of evidence-based treatments.**
- **All treatments should involve basic counselling.**
- **Psychological therapies are recommended as first line treatment for mild to moderate depression. Antidepressants are required in addition to psychological treatments for moderate to severe depression.**
- **It is important to ensure that medication is continued for a year to prevent relapses.**

mood in response to stress and/or loss. Pathologising 'normal' depression may lead to unnecessary treatments being used and the patient may come to consider normal unhappiness as an illness. For example, a depressive illness may be incorrectly diagnosed when the depressed mood is part of normal grief. This misdiagnosis may then inhibit normal grieving. Pathological or clinical depression is generally determined by its persistence (throughout the day), its duration (generally longer than two weeks) and the presence of additional symptoms. Guidelines for diagnosing depressive episodes are listed in the box on page 32.[3]

The reality, however, is that many patients with depression do not recognise that they are suffering from the condition and thus do not seek help. Their depression may be recognised only if they seek help for nonspecific physical symptoms or during a consultation for some other illness for which they are being treated. Depression can accompany a range of physical illnesses, and may be the presenting symptom of an underlying disorder such as anaemia, hypothyroidism and, in rare cases, cancer (Table 1). When it is an accompanying condition, it may have a profound effect on the outcome of illness, such as in myocardial infarction.[4] All depressed patients, therefore, should have a physical review and undergo limited investigation to exclude any underlying disorder.

The current public health approach to depression, with its greater emphasis on community education and reducing stigma, encourages people suffering from depression to recognise for themselves that they are depressed and to seek help early from their GP.[5]

The key to recognising when depression is present involves a high index of suspicion (always expect patients to be depressed), putting into practice good communication skills and explicitly asking patients whether they have been feeling depressed, feeling low or not able to get pleasure and enjoyment from activities (Table 2).[6]

Finally, an assessment of the risk of harm to self and others (especially children) is an essential part of the examination of the depressed patient and is crucial to treatment planning. Suicide or self-harm is an all too often accompaniment of depression, and the doctor needs to be constantly vigilant about the emergence of suicidal thoughts, ideas or plans. It may be anxiety provoking for both doctor and patient, and the doctor has to deal with his or her own anxiety as well as that of the patient. It is essential to see the patient alone at some point during the interview and to sensitively enquire about, and listen long enough to elicit, suicidal thoughts, plans or intent (Table 3). This is especially true if the patient is feeling slowed down, ashamed or fearful of the consequences of admitting thoughts of harm. Ask directly about

Depression in adults

PHOTOLIBRARY

Depression is both common and treatable but often goes unrecognised and undertreated. Psychological treatments are recommended as the first line treatment for mild to moderate depression; moderate to severe depression requires the addition of antidepressant drugs.

thoughts of self-harm – it does not 'put the idea' in the patient's mind – and do not apologise for asking.

Table 1. Physical conditions associated with depression

- Thyroid disease
- Autoimmune diseases
- Malignancy
- Anaemia
- Nutritional deficiencies
- Alcohol misuse

Diagnostic guidelines for depression in adults[3]

Presenting complaints

- The patient may present initially with one or more physical symptoms (e.g. fatigue, pain). Further inquiry will reveal depression or loss of interest.
- Irritability is sometimes the presenting problem.
- Some groups are at higher risk (e.g. those who have recently given birth or had a stroke, those with Parkinson's disease or multiple sclerosis).

Diagnostic features

- Low or sad mood.
- Loss of interest or pleasure.
- The following associated symptoms are often present:
  - disturbed sleep, especially waking early with feelings of anxiety or despair
  - guilt or low self-worth or loss of self-confidence
  - fatigue or loss of energy or decreased libido
  - motor restlessness or slowing of movement
  - poor concentration
  - disturbed appetite
  - suicidal thoughts or acts.
- Symptoms of anxiety or nervousness are often present.

Differential diagnosis

- If hallucinations (hearing voices, seeing visions) or delusions (strange or unusual beliefs) are present, consider an acute psychotic disorder. If possible, consider consultation about management.
- If history of manic episode (excitement, elevated mood, rapid speech) is present, consider bipolar disorder.
- If heavy alcohol or drug use is present, consider alcohol use disorders or drug use disorders.
- Some medications may produce symptoms of depression (e.g. β-blockers and other antihypertensives, H_2-blockers, oral contraceptives, corticosteroids).

Differential diagnosis

The boundary between anxiety disorders and depression is not clear, and in the primary care setting a mixed presentation is common. Anxiety is a common symptom of depression, and it is possible that the depressive component of the illness may be missed when assessing a patient. It is, important therefore, to ask anxious patients about anhedonia, loss of self-esteem, feelings of guilt and preoccupation with past misdeeds, as these are characteristic of depression and are not part of a pure anxiety disorder.

Chronically ill patients may show a low mood with reduced ability to experience pleasant events. Vegetative symptoms (for example, early morning awakening, mood worse in the mornings, poor appetite and weight loss) are difficult to interpret in these patients, particularly in the terminally ill in whom somatic complaints are complex, anxiety is common and agitation may be due to many causes. While hopelessness for his or her own predicament may be understandable, pervasive global hopelessness, preoccupation with guilt or punishment and suicidal thoughts in a patient all suggest depression.

The very early stages of grief due to the loss of a loved person, pet, job or relationship show considerable overlap with depression. Caution in diagnosing any but the most obvious case is wise. However, grief rarely encompasses thoughts of death (except in relation to the deceased), preoccupation with guilt and hopelessness, prolonged functional impairment or hallucinations (except, again, in relation to the deceased).

Subtypes of depression

It is important to recognise the different subtypes of depression, especially the melancholic type – which has a biological basis. Melancholia can vary in severity from mild to severe and is characterised by the presence of vegetative symptoms, psychomotor changes and pervasive anhedonia. Patients suffering from melancholia will require antidepressant medication (or electroconvulsive therapy [ECT] in severe cases) in addition to psychosocial treatments.

Patients suffering from bipolar disorder generally will have more depressive than (hypo)manic episodes.[7] Bipolar depression is characterised by a melancholic type of depression with significant psychomotor change or atypical depressive symptoms, especially hypersomnia and anergia.[8] The treatment response to bipolar depression tends to be poor, and may be a contributing factor to treatment resistance. It is worth considering that

patients may be suffering from bipolar depression if they are not responding to standard treatment. A past history of treatment for mania or hypomania would confirm this. Episodes of feeling elated, full of zest or energy could suggest unrecognised hypomania (bipolar II disorder). There is also a risk that antidepressants may induce a 'switch' to mania and so adjunctive mood stabilisers are required. Lamotrigine is now being suggested as the preferred mood stabiliser for patients with bipolar depression, but it is not yet indicated on the PBS for this so there is a high cost for the patient.

A comprehensive approach

In order to understand a patient's depression it is essential to take a biopsychosocial approach. Such an approach means that it is necessary to determine the biological, social and psychological factors contributing to the depression in terms of:

- the background factors predisposing the individual to become depressed
- the precipitants to the onset of the depression (the resolution of these life stressors may be an important focus for counselling)
- the factors that act to maintain the depression (for example, being in a dysfunctional relationship).

With regard to the background factors:

- biological factors include genetic predisposition, other medical illnesses and concomitant medications
- social factors include particularly social adversity, poor social support and being in dysfunctional (and/or abusive) relationships
- psychological factors include early developmental experiences (e.g. child sexual, physical or emotional abuse), personality and coping style.

Management planning

The evidence based treatments for depression have now been summarised in several clinical practice guidelines, such as those developed by the Royal Australian and New Zealand College of Psychiatrists and beyondblue.[9,10] These guidelines suggest there is evidence for the efficacy of a number of nonpharmacological therapies for mild to moderate depression and for the efficacy of the SSRIs for mild to moderate depression. For moderate to severe depression, the evidence suggests the importance of using antidepressant medication. Working in partnership with a psychiatrist is recommended for the more severe and treatment resistant depressions.

The management of depression requires a collaborative approach between the doctor and the patient. The patient needs to be informed about the diagnosis and the treatment options, and his or her treatment preferences need to be taken into consideration as these will influence treatment adherence. Information sharing is crucial and can be facilitated by providing the patient and the carers with good quality information such as the RANZCP consumer and carer clinical practice guidelines (available online at www.ranzcp.org/publicarea/cpg.asp#consumer) or directing them to websites such as those of beyondblue (www.beyondblue.org.au/), the Black Dog Institute (www.blackdoginstitute.org.au/) or depressioNet (www.depressionet.com.au).

The development of a specific treatment plan will depend on the clinical presentation (including the type and severity) of the depressive episode, an understanding of the main contributing factors to the episode of depression, and the patient's particular predicament, risk assessment and treatment preferences.

Determining treatment

The type of depression plays an important part in determining the specific treatment to be offered:

- for patients with a predominantly biological depression (melancholia and bipolar depression), antidepressant medication and psychological treatment will be required
- for patients with nonmelancholic depression, psychological therapies should be the first choice of treatment, although there is evidence for the efficacy of the SSRIs and other antidepressants.

It is important to discuss with patients the options and the pros and cons of drugs

Table 2. Keys to recognising depression

- Allow the patient to speak freely without interruption
- Listen actively and empathically
- Encourage the patient to speak about personal issues
- Explicitly ask the patient about depressive symptoms such as:
  - the inability to derive pleasure and enjoyment from activities
  - low self-esteem
  - feelings of worthlessness or guilt
  - sleep disturbances
  - appetite disturbances
  - anxiety symptoms
- Ask the patient if he or she would like help[1]

Table 3. Harm assessment in depressed patients

- See the patient alone
- Ask the patient specific questions, such as:
  - have you thought life was not worth living?
  - have you thought about killing yourself?
  - do you have any plans to end your life?
- Assess the risk of the patient harming him or herself or others (especially children)

versus nonpharmacological treatment. As mentioned before, considering a patient's preferences for treatment aids adherence.

The process of assessment – active listening and permitting the patient to speak freely (ventilation) to an empathic 'healer' – has nonspecific but very important therapeutic effects. It may be that an invitation to reflect on their circumstances after the initial interview provides some patients with enough support to induce change.

Psychological treatments are indicated for all patients with depression and should constitute the initial treatment for many patients. However, antidepressants are likely to be also needed for those with melancholia and bipolar depression. Psychological treatments have been well researched, are evidence based and may offer the patient considerable advantages in relapse prevention. The choices are described below.

- Cognitive behavioural therapy (CBT), while considered to be the treatment for everything, is the preferred therapy for patients who have clinical features that reflect disturbance in their cognitive style or who are exhibiting depressogenic behaviours (avoiding participating in activities for fear of failure). For example, patients who have low self-esteem, are oversensitive or who construe everything in a negative way will benefit from CBT.
- Interpersonal therapy (IPT) is an appropriate treatment for patients who are experiencing interpersonal conflict such as marital difficulties or work related conflicts.
- Structured problem solving is an appropriate treatment for patients who have become overwhelmed by their predicament and feel they are unable to find a solution.
- Supportive counselling is the most appropriate treatment for patients who are finding themselves without significant support and who need someone to be a sounding board to help them cope with their depression.

Elements of each type of focused psychological treatment can be applied at different times during the course of treatment in an individual patient, depending on what is happening with the patient.

If an antidepressant is to be used, the choice depends on the efficacy, safety (including potential drug interactions) and tolerability of the available drugs and the patient's preference. The newer classes of antidepressants, the selective serotonin reuptake inhibitors (SSRIs), the serotonin and noradrenaline reuptake inhibitors (SNRIs), the noradrenergic and specific serotonergic agents (NaSSAs) and the selective noradrenergic reuptake inhibitors (NARIs), are safer in overdose than the tricyclic antidepressants (TCAs) and the monoamine oxidase inhibitors (MAOIs). However, this should not preclude the use of the older antidepressants if they are clinically indicated.

In general, it is probably better to use the SSRIs for mild to moderate depression where they have proven safety and effectiveness, although they do have significant side effects. The dual action (serotoninergic and noradrenergic) antidepressants, such as the SNRI venlafaxine (Efexor) and the NaSSA mirtazapine (Avanza, Axit 30, Mirtazon, Remeron) and some of the TCAs, have greater efficacy for melancholia and severe depression than other antidepressants. The selective NARI reboxetine (Edronax) is of benefit when patients experience psychomotor retardation and require activation. If a patient has responded to a particular antidepressant previously then it should be used again.

It is important to discuss with patients the options and the pros and cons of drugs versus nonpharmacological treatment. As mentioned before, consideration of the patient's preference for treatment aids treatment adherence.

'Better outcomes in mental health'

The Commonwealth initiative 'Better outcomes in mental health' provides rewards to GPs (in the form of a service incentive payment) for using a '3-step mental health process' for the management of the common mental health problems. The process includes an assessment, a mental health plan and a review. Details about this initiative are available from the Australian Division of General Practice (www.adgp.com.au).

When to refer to a psychiatrist

Patients may be referred to a psychiatrist for an opinion or ongoing management. A new MBS item number allows GPs to refer patients to a psychiatrist for an opinion, with the psychiatrist providing a management plan back to the GP. Reasons for referral include:

- severe symptoms
- depression complicated with physical illness
- depression complicated by personality problems
- depression nonresponsive to treatment
- concerns about suicide
- psychotic (delusional) depression
- bipolar disorder (bipolar depression)
- discomfort in managing the patient.

Patients who have a psychotic depression or are at risk of suicidal behaviour need urgent assessment and treatment, and may require referral to a hospital under the Mental Health Act.

Psychological treatments

Structured problem solving

Structured problem solving allows a structured approach to patients 'stuck' or overwhelmed by life difficulties. A number of carefully defined problems are identified, all possible solutions are 'brainstormed', and each possible solution is discussed. The patient and therapist choose a solution to attempt, a detailed plan is developed and the patient is encouraged to carry out the plan. How the plan was carried out is reviewed, the solution is re-evaluated as necessary and further efforts are encouraged.

Interpersonal therapy

IPT aims to remove symptoms and prevent relapse and recurrence. It does not attempt to define the cause of a depressive episode but uses the connection between current life events and mood disorder to help the patient understand and deal with his or her episode of illness. IPT is based on research findings on the psychosocial and life events aspects of depression that have demonstrated the relationship between depression and the four domains of IPT: loss, role disputes, role transitions and interpersonal deficits. The overall strategy is that by solving an interpersonal problem the patient will improve his or her life situation and relieve the symptoms of the depressive episode. IPT treatment lasts 12 to 16 sessions and there is good evidence for its efficacy in major depression.

Cognitive behavioural therapy

CBT is based on the premise that depressive thoughts are induced by, but also induce, a depressed mood. Studies show the thinking of depressed people to be dominated by self-derogation, negative expectations, overwhelming problems and responsibilities, deprivation and loss, and escapist and suicidal wishes. Beck suggested that recovery from depression could be achieved by teaching patients to re-evaluate everyday thoughts and to understand the longstanding belief systems underlying them.[11]

CBT is a goal orientated therapy, an active treatment that encourages optimism about change. Treatment proceeds through the stages:

- problem identification
- specific cognitive interventions designed to reduce the frequency of negative thoughts, behavioural and motivational deficits
- monitoring and questioning of negative automatic thoughts
- relapse prevention.

There are many self-help manuals available on CBT, and there is also an effective evidence based self-help program online (MoodGym, formulated by the Centre for Mental Health Research at the Australian National University; http://moodgym.anu.edu.au).

Supportive counselling

Supportive counselling is helpful for many patients who may be unable to deal with the stresses they confront. It is helpful to be able to discuss and talk through these stresses with a nonjudgemental and empathic person. The purpose of such counselling is to allow patients to come up with their own solutions (with encouragement to consider other options) and not be just given advice.

Pharmacological treatments

Real differences in the efficacy of the antidepressants remain uncertain, although those with dual action (serotonergic and noradrenergic) are considered preferable for melancholic or the more severe types of depression. As mentioned earlier, the choice of medication depends on the tolerability, safety, potential drug interactions, patient preferences and type of depression.

Critical issues in the pharmacological management of depression are ensuring that the dose of medication and the duration of treatment are adequate. All antidepressants require use for at least two weeks to achieve a good clinical response, and it is essential to ensure that the patient understands this. It is worth scheduling regular visits during the early stages of treatment as patients can become demoralised when they are not getting an instant 'cure'. All too often patients will stop their medication once they are in remission, and they are then at risk of having a relapse. It is generally recommended that patients continue taking their antidepressant for a year before ceasing treatment.

SSRIs

The SSRIs are the most widely used of the antidepressants and are now considered to be the first line antidepressant for mild to moderate depression. They have the distinct advantages of having a simple dosing regimen and being generally safe. When they were first introduced, their advantage was their side effect profile compared with the TCAs. With 15 years of experience of using SSRIs, it is now apparent that some of their side effects can be troubling for the patients, particularly the sexual side effects (such as decereased libido and delayed or absent orgasm). Of note, it is recognised that SSRIs can cause agitation during the first weeks or so of treatment, which could precipitate suicidal thoughts. Any patients being started on an SSRI should be warned about this; use of a benzodiazepine can help in reducing the agitation. A marked withdrawal syndrome occurs with some of the SSRIs, particularly paroxetine, and doses need to be tapered with these drugs.

Dual action antidepressants

The SNRI venlafaxine and the NaSSA mirtazapine can be highly effective, especially for melancholia. Venlafaxine carries a risk of hypertension as well as side effects of nausea, vomiting and dizziness on both initiation and withdrawal (the withdrawal syndrome can be particularly severe), and it can be lethal in overdose. Mirtazapine is often sedating and causes significant weight gain.

Duloxetine is a new SNRI that, in addition to its antidepressant effectiveness and favourable side effect profile, has a beneficial effect on pain syndromes. It is not yet approved for use in Australia, although TGA approval is expected this year.

NARIs

Reboxetine, a selective NARI, is an activating antidepressant that is useful in severe depressions with prominent retardation. It needs to be introduced slowly as many patients have difficulty with anxiety and agitation.

TCAs

TCAs are highly effective antidepressants, now generally regarded as second or third

line choices since the introduction of the SSRIs.[12] Their anticholinergic side effects can be burdensome and they can be lethal in overdose, but they are still useful antidepressants, especially for those with a melancholic depression. A problem with the tricyclics has been that underdosing is common; it is generally considered that 150 mg per day is required to achieve a full therapeutic response, although there are patients who benefit from lower doses.

Other agents

Other medications used to treat depression include the MAOIs and augmentation strategies such as lithium (Lithicarb, Quilonum SR) and anticonvulsants. MAOIs should be used with caution in general practice because, although they are effective and safe antidepressants, they require the patient to be on a low tyramine diet to avoid a hypertensive crisis.

St John's Wort is increasingly being used as an over-the-counter antidepressant and is supported by some evidence of its efficacy in mild depression, although this is not as clearcut as was previously thought. It is considered attractive by patients as it is regarded as a 'natural' therapy; however, it does have side effects and some drug interactions. It is important to enquire about its use to avoid any interactions.

ECT is still the most effective (and safe) antidepressant therapy for severe, intractable depression; however, it should be used only in specialist units where appropriate monitoring can take place.

Conclusion

Depression is a common treatable disorder. Therapist optimism is appropriate and treatment of depression can be highly rewarding. It is crucial not to underestimate the profound effect even mild depression can have on the quality of life of an individual and his or her family. MT

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Depression in women
aetiological factors and treatment implications

The greater vulnerability of women to depression than men is related to factors either exclusive to or more likely to affect women than men. Many of these factors act at specific times in a lifetime and therefore the particular life phase a patient is in has specific implications for treatment of her depression.

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It is a universally acknowledged fact that depression is more common in women than men. It is also clear that women with depression across life phases have particular needs in terms of treatment. This article outlines epidemiological and clinical issues pertaining to depression in women, and suggests 'female sensitive' treatment approaches.

Female vulnerability to depression

Females are about twice as likely as males to experience depression during their lifetimes. This finding applies to depressive symptoms as well as case-level depressive disorders and holds across different ethnic and cultural groups, suggesting that biological rather than societal factors are the major determinants. Higher rates of psychiatric problems in women are not limited to depression but also apply to anxiety, somatisation, eating disorders and other related comorbid disorders.

The gender gap in depression emerges at puberty, such that by the age of 15 years females are twice as likely as males to have experienced a major depressive episode. One hypothesis is that the vulnerability of females to depression lies in

IN SUMMARY

- **Females are about twice as likely as males to experience depression during their lifetimes, and it is likely that biological rather than societal factors are the major determinants.**
- **An SSRI is usually effective in treating women of all ages with depression. However, the particular life phase a depressed woman is in has specific implications for treatment.**
- **During pregnancy, there has to be a balance between the risks associated with the depression itself and the risks of any treatment. The risk of teratogenicity with SSRIs and TCAs is very low.**
- **No specific antidepressant treatment is usually required for postpartum blues. For postnatal depression, the risk of breastfeeding while taking an antidepressant needs to be addressed; psychotherapy and social support can be effective adjuvants to medication. Immediate referral to a specialist mental health service is required for postpartum psychosis.**
- **Antidepressant use in the menopause should be guided by illness severity and whether a particular agent has helped in any earlier depressive episodes.**
- **Antidepressant use in the elderly needs to take into account the changes in metabolism that occur with increasing age, as well as a reduced tolerability to medications because of concomitant physical disorders.**

continued

PHOTOLIBRARY

'the domain of developmental psychopathology, and specifically those developmental processes associated with early adolescence'.[1] This view encompasses both evolutionary factors that are linked to reproductive biology and psychosocial risk factors that emerge during the reproductive years. Other biological and social factors emerging in later life serve to accentuate the female risk for depression. These factors are either exclusive to or more likely to affect women than men, and include:

- hormonal flux associated with the menstrual cycle, the pregnancy and postpartum periods and the menopause[2]
- traumatic events, such as rape and domestic violence
- social status, such as financial dependency and discrimination
- loss life events, such as pregnancy loss, loss of a spouse and the empty nest syndrome.

Thus, inherent vulnerabilities interact with psychosocial issues across a woman's lifespan to render her prone to depressive disorders. The particular life phase the patient is in has specific implications for treatment.

Perimenstrual mood symptoms

Many women, but notably those under 25 years of age, experience some degree of mood disturbance in the week to days preceding their menstrual period. In some 5% of women, these symptoms are recurrent and severe enough to warrant a diagnosis of premenstrual dysphoric disorder. Typical symptoms include depressed mood, anxiety, affective lability, irritability, loss of energy, changes in sleep pattern and feelings of bloating and breast soreness. The symptoms abate within a few days of the onset of the menses.

Management includes taking an accurate history and asking the patient to keep a symptom diary throughout the menstrual cycle, paying particular attention to changes around menstruation. General lifestyle strategies, including sleep regulation, relaxation and attention to nutritional factors such as avoidance of caffeine, can be helpful.

In terms of medication, the relative specificity of benefit from serotonergic antidepressants such as the selective serotonin reuptake inhibitors (SSRIs) and the tricyclic antidepressant (TCA) clomipramine (Anafranil, Placil) in this clinical disorder suggests an underlying serotonergic dysfunction. Treatment with SSRIs, generally in the standard dose ranges, is usually well tolerated, although some women experience sexual dysfunction, which can create its own difficulties. Weight gain associated with some antidepressants (for example, the serotonergic tetracyclic agent mirtazapine [Avanza, Axit 30, Mirtazon, Remeron]) can be particularly worrisome for many women, and this should be considered when choosing an antidepressant. Some women prefer intermittent dosing in the luteal phase, such that they take their antidepressant only when symptomatic, but this strategy is not generally required and can raise problems with withdrawal effects, especially when shorter acting antidepressants are taken.

Hormonal treatments have also been evaluated in premenstrual dysphoric disorder. It seems that oestradiol might have a role, but the results are conflicting. The evidence base for progesterone is not very compelling, although Primolut N (norethisterone) is available on the PBS for premenstrual syndrome.

Depression during pregnancy

Around 10 to 20% of women experience a depressive episode during pregnancy; this in turn is a strong predictor of postpartum depression. Clinical judgement is required to differentiate 'normal' concern about impending motherhood and clinical depression. Symptoms can be interpreted as part of pregnancy (for example, fatigue, somatic symptoms, appetite disturbance and loss of libido), and treatable depression can be missed. The clinician needs to elicit the core depressive symptoms of anhedonia, sleep disturbance, low self-esteem and appetite changes. Early morning wakening and melancholic features such as worsening of mood in the mornings are specific pointers for active pharmacological intervention. The presence of suicidal or psychotic thoughts is particularly serious and usually requires hospital admission.

Treatment of depression during pregnancy is complicated by concerns regarding the potential adverse impact of antidepressants on the developing fetus. Also, there are studies suggesting that untreated depression during pregnancy is associated with low birthweight and increased risk of preterm delivery.[3] Hence, the balance is between the risks associated with the depression itself and the risks of any treatment offered. The decision making process must include a full discussion with the woman and (where appropriate) her partner, and the treatment plan should be fully documented for each phase of the pregnancy and for after delivery. Data exist, although not from randomised controlled trials, that suggest the risk of teratogenicity with SSRIs and TCAs is very low; other antidepressants carry a slightly higher risk warning.[4] Also, there is no compelling evidence of any heightened risk of long term developmental or intellectual impairment in children who had been exposed to antidepressants *in utero*.

In general, if it is thought that treatment with an antidepressant is warranted, the lowest effective dose should be used and polypharmacy avoided to minimise exposure of the fetus. It is sensible to avoid agents that are likely to worsen the physical symptoms of pregnancy; for example, many TCAs cause or worsen fatigue and constipation. Also, it is as well to avoid agents with a long half-life, as this limits neonatal toxicity (which has been reported, for example, with fluoxetine). On the other hand, agents associated with withdrawal effects, such as paroxetine and venlafaxine, are potentially more likely to produce such effects in the neonate.

Discontinuation of antidepressants during pregnancy is associated with a high risk of depressive relapse. Similarly, the decision to continue maintenance therapy has to be based on the risk–benefit ratio of treatment versus the likelihood and probable severity of illness relapse. A specialist opinion should be sought for complex cases or if other psychotropics are being considered (for example, mood stabilisers).

Postpartum mood disorders

Postpartum blues

Many women experience some mood symptoms in the postpartum period.[5] By far the most common is the so-called 'blues' that affects up to 85% of mothers in the first few weeks after delivery. Symptoms begin within the first postpartum week and include tearfulness and feelings of not being able to cope. These symptoms resolve by around day 12, and require no specific treatment apart from reassurance and general advice about maintaining physical and emotional health.

Postpartum depression

If depressive symptoms persist and/or become more severe, a diagnosis of postnatal depression (PND) must be entertained. PND is thought to affect 10 to 20% of women. Screening using the 10-item Edinburgh Postnatal Depression Scale, which controls for items such as the sleep disturbance that is part of early parenthood, is widely used to detect 'cases' of PND and ensure early intervention.[6] Early detection and intervention are important because depression in the mother can affect infant bonding and wellbeing, and in severe cases lead to tragic outcomes such as suicide (rare during this phase of life – probably an inbuilt 'protective' mechanism) and infanticide.

Treatment of PND involves a careful discussion of risks and benefits with the mother and her partner. In particular, the risk of breastfeeding while taking an antidepressant needs to be addressed, although the risks are low for most agents, including SSRIs and TCAs. Agents that should probably be avoided while breastfeeding include fluoxetine because of its long half-life and doxepin as it can potentially cause respiratory depression in the neonate. Supportive counselling, cognitive behavioural therapy and interpersonal psychotherapy have also been shown to be effective in the treatment of PND, and can be usefully employed in conjunction with medication. Social support such as PND support groups can also be of benefit, particularly where social isolation is perpetuating the depression. Attention should also be given to the male partner, and appropriate support and counselling offered to address role transition and marital issues.

In severe PND, electroconvulsive therapy might be required. Usually this is reserved for women who are not responsive to antidepressant medication and/or in whom oral intake is compromised, or for those who are actively suicidal.

Postpartum psychosis

Postpartum psychosis is a much more severe form of mood disorder, occurring in around one in 500 live births. Onset is usually abrupt, the presentation is one of a manic-like psychosis, and it is thought to be aetiologically and clinically linked to bipolar disorder.[7] In some women it can present as a confusional psychosis, and in others as a severe psychotic depression. Whatever the particular clinical features, this is an extremely dangerous psychiatric emergency, with a very real risk of suicide and/or infanticide. Particular vigilance is needed in women with a personal or family history of bipolar disorder, or in whom a previous postpartum psychosis has occurred (the risk of recurrence in subsequent pregnancies is around 50%).

Immediate referral to a specialist mental health service is required. Inpatient treatment, preferably in a mother–baby unit, is usually warranted, and involuntary admission may be necessary to ensure safety and appropriate treatment. Treatment with antipsychotics and/or mood stabilisers is usually required, with ECT being used in very severe cases needing rapid response. Support for the partner should be offered, and every effort made to ensure there is as little disruption as possible to the mother–baby bonding process, obviously with close monitoring to ensure safety.

Ongoing treatment with a mood stabiliser may be appropriate, and counselling of the couple regarding risk of recurrence of a bipolar episode (particularly in the event of a future pregnancy), as well as the risk associated with the use of mood stabilisers during pregnancy, is critical. The latter issue is beyond the scope of this article, but the reader is referred to Misri and colleagues (2006) and Dodd and colleagues (2006) for a detailed exposition.[4,8]

Depression in the menopause

There is little doubt that the menopause is an important phase in the life of a woman. Not only does it emphasise loss of fertility, but it is also associated with a variety of somatic symptoms, including hot flushes, night sweats and vaginal dryness leading to dyspareunia. There are often associated psychosocial changes as well, including children leaving home and a realigned relationship with a spouse, and a redefining of career goals. Physical health problems might also start to express themselves.

The relationship between menopause and depression has, however, been somewhat controversial, not least because of difficulties in determining the precise timing of the menopause, and a variety of other methodological problems. In a comprehensive review of both cross-sectional and longitudinal studies, Dennerstein and Alexander (2006) concluded that most women do not experience depression during the menopausal transition, but it is a particularly vulnerable time for some.[9] Risk factors for depression at this time of life include a prior history of depression, PND or premenstrual dysphoric disorder, lack of social supports, interpersonal and other stressors, and physical health problems. Women with a prolonged menopausal transition or who undergo surgical menopause may also be at heightened risk.[10] Symptoms range from mild to severe, and include in particular feelings of loss of ability to attend and concentrate, memory loss, anxiety, tearfulness and irritability.

The treatment of depression in the menopause requires a sympathetic awareness of the psychosocial context referred to above. Physical symptoms such as hot flushes should be addressed (for example, through teaching paced breathing). Antidepressant use should be guided by illness severity and whether a particular agent has helped in any earlier depressive episodes. It seems that venlafaxine (Efexor) has benefit for hot flushes as well as low mood, and that possibly paroxetine (Aropax, Oxetine, Paxtine) and fluoxetine (Auscap, Fluohexal, Fluoxebell, Lovan, Prozac, Zactin) have similar benefits. Other antidepressants may also be useful, such as mirtazapine and the TCAs.

The use of oestrogen replacement therapy is particularly controversial, given the physical health risks involved, including thromboembolism and breast and endometrial cancer. However, the short term use of oestrogens (in conjunction with progesterone if the woman has an intact uterus) may be warranted in some cases of mild depression; there should be detailed discussion with the woman about the benefits and risks before a decision to use hormone therapy is taken. The benefits of oestrogen in augmenting antidepressant response have not been conclusively shown.

Depression in old age

In most societies, women outlive men and represent the majority of the elderly population. There is a misconception held by the aged themselves as well as by health professionals that depressed states are a normal part of ageing, leading to underdetection and undertreatment of depression in the elderly. The elderly remain a high risk group for suicide, usually in association with depression.

It is thus important for clinicians to have a high index of suspicion for depression in elderly people, particularly those with social and physical risk factors such as bereavement, social isolation, carer burden, poor nutrition and failing physical health. The symptoms of depression in the elderly do not differ markedly from those in younger patients, although subjective complaints of memory loss and somatic symptoms are more common. The considerable overlap between depression and dementia needs to be considered as elderly depressed patients with cognitive problems may have not only more severe depression but also an increased risk of developing dementia subsequently.

In approaching the treatment of an elderly depressed woman, particular attention needs to be paid to the psychosocial context, and attempts should be made to address perpetuating factors like appropriate housing, linkages to community services and social supports. For example, socially isolated patients can be encouraged to attend day centres and undertake activities that they used to enjoy but have 'given away' with age. The interaction between physical health problems and mood problems needs to be borne in mind, and physical health should be monitored and optimised. Particular attention should be paid to chronic pain and chronic diseases because these are risk factors for suicide.

Psychological approaches to depression in the elderly are not widely used, perhaps due to a feeling among clinicians that they are not applicable in this age group. In fact, cognitive behavioural therapy has been shown to be effective in the depressed elderly, especially if therapists have been trained specifically in working with this age group.[11] Other effective psychological techniques include creative reminiscence and interpersonal therapy; the latter can be particularly useful for spouse bereavement.[12]

Gender-specific differences in drug pharmacokinetics, due to the effects of female hormones on, for example, body mass and lean muscle to fat tissue ratio, become more prominent in older women. The use of antidepressant medication in the elderly needs to take into account the

changes in metabolism that occur with increasing age (usually drug clearance rates are slower), in addition to reduced tolerability to medications because of concomitant physical disorders. For a given dose, elderly women are more likely to have higher plasma levels of antidepressant and greater risk of adverse effects. SSRIs are usually the first choice of antidepressant for the elderly, as they have minimal antimuscarinic, antihistaminergic and antiadrenergic side effects. Drug interactions are particularly problematic in the elderly as these patients are often already taking several other medications. Thus, it is prudent to use the 'cleanest' antidepressants (in terms of side effects and drug interactions) with a shorter half-life. Citalopram, escitalopram (Lexapro) and sertraline (Concorz, Eleva, Xydep, Zoloft) would seem sensible choices in this regard.

Usual starting doses of antidepressants in the elderly are half the usual adult dose, with gradual dose increment if required. The use of psychosocial therapies in combination with antidepressants may optimise responses.

Conclusions

Women are at particular risk for depressive symptoms and disorders from adolescence to old age. The reasons behind this are complex, but encompass biological and psychosocial domains. Treatment interventions for depressed women need to take account their life stage as well as their reproductive phase and psychosocial context. MT

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DECLARATION OF INTEREST: Professor Castle has received grant monies from Eli Lilly, Janssen-Cilag, Roche, Allergan and Bristol-Myers Squibb, and travel support and honoraria for talks from Eli Lilly, Bristol-Myers Squibb, AstraZeneca, Lundbeck, Janssen-Cilag, Pfizer, Organon and Sanofi-Aventis; and he is, or has been, an advisory board member for Lundbeck (Lexapro), Eli Lilly (Zyprexa), Bristol-Myers Squibb (Abilify) and AstraZeneca (Seroquel).

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On the (examination) couch: psychotherapy for depression in general practice

Psychotherapeutic treatments can be matched to individual patient requirements and delivered effectively in general practice.

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Depression, which is one of the most common problems encountered in general practice, tends to be a chronic, recurrent disorder. Research suggests that short term psychotherapies work as effectively as antidepressants in treating mild to moderate depression and can be delivered effectively in primary care settings.[1-4] When given an option, patients tend to prefer psychotherapy.[5] Yet a recent database review of Australian general practices showed that over 90% of patients diagnosed with depression are prescribed antidepressants, with few receiving a recognised depression-specific psychotherapy.[6]

What are the barriers to using psychotherapy in general practice? Obvious ones include time pressures and the lack of availability of accessible training and support. However, other factors also appear to be at work. A recent survey of 420 Australian GPs yielded some interesting results.[7] Non-pharmacological therapies (psychotherapies) were much more likely to be used by female GPs, GPs in urban areas and those who had undertaken additional mental health training. More generally, GPs who feel better able to distinguish between depression and unhappiness and who find treating patients with depression rewarding are more likely to initiate psychotherapeutic treatments.[8]

This article summarises psychotherapies that are available in general practice and makes some clinically informed suggestions about matching treatments to individual patients.

What is psychotherapy?

Psychotherapy has been defined as an interpersonal process designed to bring about modifications of feelings, cognitions, attitudes and behaviour that have proved troublesome to the person seeking help from a trained professional.[9] Michael Balint, the Hungarian-born British psychoanalyst, recognised that every doctor–patient encounter is inherently psychotherapeutic. Empathy, thoughtfulness, a positive regard for the patient and willingness to

IN SUMMARY

- **Patients prefer psychotherapy. It should be considered as a first line treatment in uncomplicated mild or moderate nonmelancholic depression.**
- **Supportive counselling, cognitive behavioural therapy (especially problem solving) and interpersonal psychotherapy have been shown to be effective in primary care settings.**
- **Short forms of interpersonal psychotherapy and cognitive behavioural therapy (four to six 30 minute sessions) have been developed for general practice.**
- **Add a first line antidepressant if no benefit after four to six sessions.**
- **Substance abuse, a personality disorder or acute intercurrent stressor should be excluded in patients who do not respond to psychotherapy.**
- **Specialist review is indicated for patients with suicidal ideation, mania or psychosis, and for patients with progressive or treatment-resistant depression.**

hear his or her story are the foundations of any good psychotherapeutic relationship.

How effective is it?

Research in psychotherapy is methodologically complex, and it is difficult to conduct studies of adequate power and duration because there is no incentive for large pharmaceutical companies to fund them. Nevertheless, the results of existing research are surprisingly consistent, showing that skillfully delivered, depression-specific psychotherapies are as effective as antidepressant medication for mild to moderate depression.[10] Overall, about 50% of patients receiving psychotherapy alone will achieve full remission of symptoms, but about half of these will develop recurrent symptoms after one year without some kind of maintenance treatment. These figures may sound disappointing, but they are very similar to those seen in longer term trials of antidepressants and reflect the fact that depression tends to be a recurrent or persisting disorder for many people.

What types of psychotherapy are available?

More than 400 schools of individual psychotherapy have been described, but it is helpful to think of them as occurring within three streams:

- **Counselling and supportive psychotherapies (sporting analogy: beach cricket).** Like beach cricket, counselling and supportive psychotherapies can begin spontaneously with a minimum of equipment. The primary requirements for both endeavours are goodwill, enthusiasm and a bit of space.
- **Structured psychotherapies (sporting analogy: one-day cricket).** These include cognitive behavioural therapy (CBT) and interpersonal therapy. Like one-day cricket, they are highly structured, time-limited and require the acquisition of specific skills and regular coaching.
- **Intensive psychotherapies (sporting analogy: test cricket).** These tend to be longer term therapies, and aim to achieve far-reaching changes in personality and attachment style. Like test cricket, they are redolent of a more sedate age: seemingly inconsistent with the pace of modern life, somewhat unfashionable, and having no guarantee of a positive outcome. They are full of arcane lore known only to initiates, and are really vocations to which a practitioner needs to devote the majority of a working lifetime.

A guide to selecting a psychotherapy is presented in the flowchart on page 44, and the key features of the types discussed in this article are summarised in the Table.

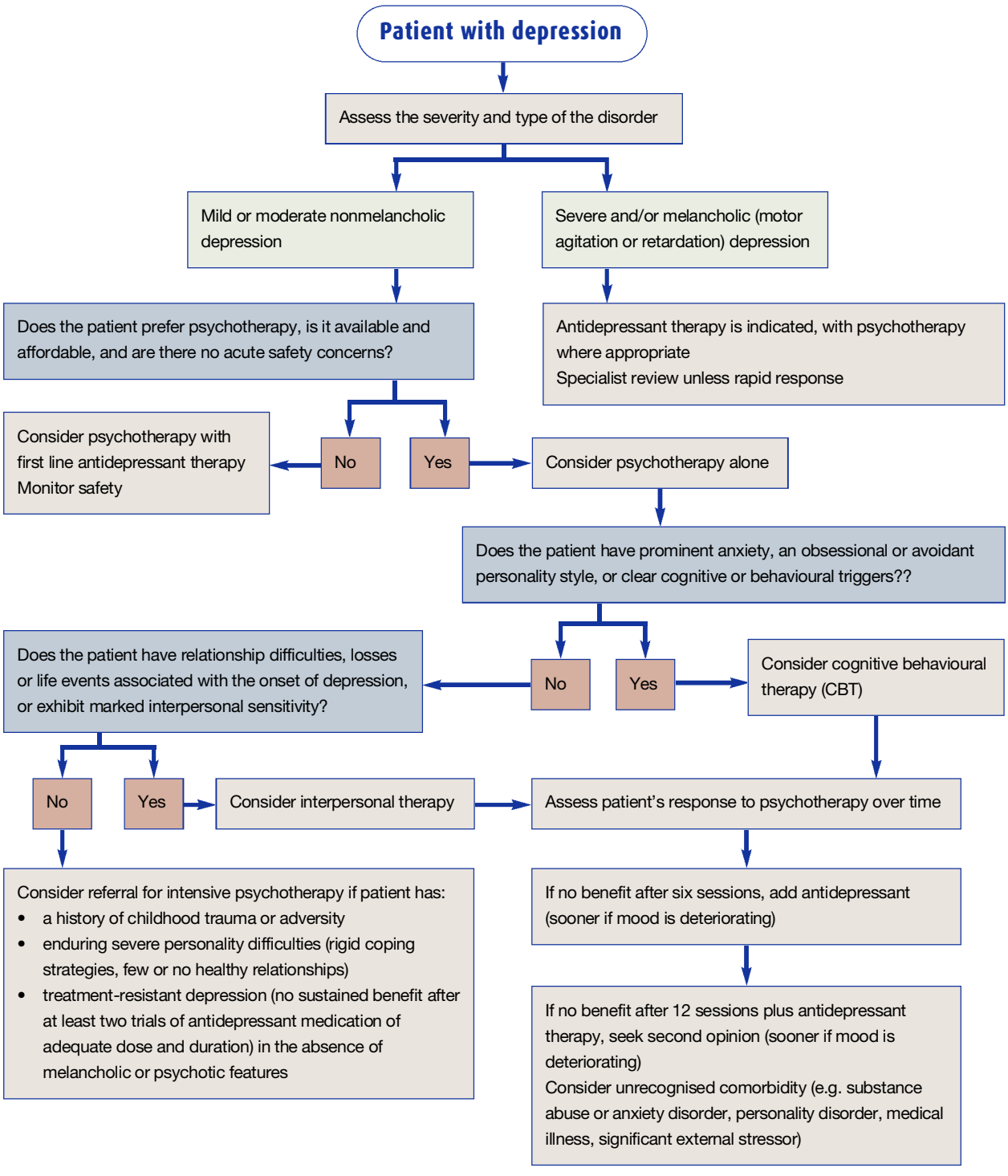
Counselling and supportive therapy

Most GPs engage in some form of counselling. Examples include encouraging patients to increase their physical activity and social contacts or to reduce drug and alcohol use, and educating them about sleep hygiene and problem solving strategies.[2,10] In this article, the terms counselling and supportive psychotherapy are used as near-synonyms, but they can be seen, respectively, as the directive (active) and supportive (containing) ends of nonspecific psychotherapy. Supportive therapy is best thought of as thoughtful and practical advice given to a person in emotional distress, with an additional 'halo' effect conferred by the patient's perception of the doctor as a respected and impartial source of help. In psychological jargon, supportive therapy 'emphasises the mobilisation of strengths to enhance self-esteem and utilise adaptive defences and positive coping skills'.[10,11]

These approaches have long been regarded with disdain by practitioners of more structured

continued

An approach to choosing a psychotherapy for depression



psychotherapies, but research has shown that many patients achieve significant improvements in depressive symptoms and interpersonal functioning. They may be particularly useful for people whose symptoms are related to an acute stressful event and for those with poor social functioning and limited insight that preclude more intensive therapies. In syndromal depression, however, studies suggest that benefits are modest and not sustained.[2,4]

Cognitive behavioural therapy

CBT, as the name suggests, is a synthesis of behavioural techniques such as operant conditioning, in which depression reinforcing habits are discouraged while more active and pro-social behaviour is encouraged, and cognitive theory, which assumes that unhelpful styles of thinking reinforce depression and require challenge. Common CBT strategies used in depression include identifying and challenging cognitive distortions, behavioural activation, structured problem solving and, where anxiety is also present, controlled breathing and progressive muscle relaxation. There is a strong evidence base for the effectiveness of well delivered cognitive behavioural interventions in depression of mild to moderate severity. A brief format (four to six sessions of 30 minutes) has been adapted for GPs by a group at the University of California, San Diego.[3]

A Cochrane review has shown specific evidence for the effectiveness of problem solving for treating depression in general practice.[12] This involves the patient formulating a problem in his or her life in clear and unambiguous terms (e.g. 'My husband is having an affair' or 'I hate my job') and then generating as many potential solutions as possible, no matter how outlandish or impractical they might seem. The patient and therapist then review the pros and cons of each suggested solution before deciding which one to implement. The outcome is reviewed and, if necessary, alternatives are generated.

Mindfulness-based cognitive therapy, which borrows a number of stress reduction techniques from meditation and Zen Buddhism, has received considerable publicity recently. It has shown benefit for stress management and as a specific treatment for depression in several small studies.[4,13] It may have specific utility in relapse prevention.

GPs interested in learning more about CBT can do so through the Better Outcomes in Mental Health initiative of beyondblue (www.beyondblue.org.au) or by contacting SPHERE, a national mental health project (www.spheregp.com.au). Excellent material is also available through the Black Dog Institute's GP workshops, part of the 1301MH initiative (accessed through www.racgp.org.au/mentalhealth), as well as the Mental Health Standards Collaboration (www.racgp.org.au). Individual or group supervision in CBT can be accessed through State or Territory branches of the Royal Australian and New Zealand College of Psychiatrists or the Australian Psychological Society.

Interpersonal therapy

Interpersonal therapy was initially developed as a time limited, weekly therapy for depression, relating patients' symptoms to difficulties in their relationships. It uses a more flexible approach than CBT and is more similar to psychodynamic psychotherapy than CBT.

In interpersonal therapy, depressive symptoms are related to one of four problem areas: grief and loss, role transitions, interpersonal disputes, and interpersonal sensitivity. After taking a careful history and establishing the diagnosis of depression, the therapist assists the patient in making an inventory of significant relationships. Several of these relationships are then discussed in detail, focusing particularly on areas of difficulty, differing expectations and indirect communication. Using a variety of techniques, including communication analysis and role play, possible solutions to interpersonal difficulties are explored. Interpersonal therapy borrows freely from other psychotherapies, but it focuses on current rather than past relationships and the therapist takes an active and directive stance. Further information can be found on the website of the International Society for Interpersonal Psychotherapy (see www.interpersonalpsychotherapy.org).

A brief form of interpersonal therapy (four to six sessions of 30 minutes), known as interpersonal counselling, has been developed, which is tailored for use in general practice.[14] GPs in New South Wales and Victoria who are interested in training and supervision in interpersonal counselling can contact Associate Professor Kay Wilhelm at the School of Psychiatry, University of New South Wales, Sydney, and Professor Fiona Judd at the School of Rural Health, Monash University, Melbourne, respectively.

Intensive psychotherapies

Intensive psychotherapies, which are also known as psychodynamic or insight-oriented psychotherapies, aim to alter fundamental aspects of personality structure. The patient is seen frequently (at least weekly) and usually for a prolonged period (for at least six months and sometimes several years), although short term dynamic therapies have been developed. Intensive psychotherapies often focus on trauma in early life, particularly attachment disruptions with caregivers. Conflicts are often acted out in the sessions, and the therapist's analysis of unconscious feelings evoked in both the patient and therapist (transference and counter-transference, respectively) is an important aspect of treatment.

The evidence for the cost effectiveness of these treatments in uncomplicated depression is limited, but it should be remembered that there are formidable barriers to conducting research in this area because of the many potential variables in patient, treatment and therapist and the difficulty in identifying the 'active' element of therapy. There is, however, accumulating

continued

evidence that these approaches may be appropriate for patients with treatment-resistant depression, a comorbid personality disorder or a history of childhood trauma, for whom both pharmacological treatments and short term psychotherapies lead to little sustained benefit.[4] For such patients, referral to a psychodynamically-trained psychiatrist, GP or nonmedical therapist should be discussed for assessment of their suitability for intensive psychotherapy.

Summary

Patients consistently express a preference for psychotherapeutic treatment of mild to moderate depression over pharmacotherapy, but the pressures of time, cost and availability militate against this. Interested

Table. Psychotherapy: what to use, and for whom*

Patient profile	Duration	Requirements	Techniques	Goals
Counselling and supportive therapy				
Patients with depressive symptoms associated with an acute stressful event, poor social functioning or limited insight	4 to 16 sessions, weekly	Empathy, common sense, positive regard for the patient	Empathic reflection, concrete advice	Enhanced self-esteem, initiation of positive changes, emotional expression
Cognitive behavioural therapy (CBT)				
Patients with mild or moderate depression, especially if comorbid anxiety or obsessional traits are present	4 to 16 sessions, weekly	Additional training, supervision	Identification of core beliefs, behavioural activation, structured problem solving; controlled breathing and progressive muscle relaxation (for associated anxiety)	Correction of cognitive distortions and dysfunctional core beliefs, modification of 'depressogenic' behaviours
Interpersonal psychotherapy				
Patients with mild or moderate depression, especially those experiencing relationship difficulties, interpersonal conflict, grief and loss, role transitions or interpersonal sensitivity	4 to 16 sessions, weekly	Additional training, supervision	Relationship inventory, problem identification, communication analysis	Improved communication, adjusted interpersonal relationships
Intensive psychotherapy				
Patients with a personality disorder or history of childhood trauma or adversity, selected patients with treatment-resistant depression	Frequent sessions, at least weekly, over more than 16 weeks	Formal training, rigorous supervision and peer group review; possibly personal therapy	Exploration of early life trauma, analysis of defence styles, transference monitoring	Development of insight, adoption of mature defences, reduced self-defeating behaviours, achievement of acceptance

* Adapted from reference 15.

GPs can receive training and supervision in a depression-specific psychotherapy, or consider developing a referral network of practitioners. Counselling or supportive therapy may be helpful for patients with acute adjustment difficulties and for those who are unable to be engaged in more structured therapies. Cognitive behavioural techniques, especially problem solving, and interpersonal psychotherapy are effective in treating depression in general practice settings, but patients may require less frequent 'maintenance' sessions to achieve enduring benefits. Finally, in patients who do not respond to structured psychotherapy, consider addition of an antidepressant, exclusion of a comorbid disorder, review by a psychiatrist, and referral for intensive psychotherapy. MT

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DECLARATION OF INTEREST: None.

Meeting the challenge of suicide prevention

All GPs should possess the clinical skills to make a general assessment and management plan for a person who is suicidal, although they should not feel obliged to continue the management. Standard treatments for psychiatric conditions that often involve suicidal behaviour are effective at preventing such behaviour.

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Between years 1997 and 2003 (the latest year for which figures are available) there was a reduction of about 20% in the number of suicides in Australia (Table 1).[1] This has probably been largely attributable to better recognition and management of mental disorders by GPs, who provide most services for those afflicted with these disorders. While this improvement is gratifying, continuing vigilance and the application of standard treatments for psychiatric conditions that involve suicidal behaviour should ensure further reduction of suicide in the future.

Causes of suicide

There are many theories about the causes of suicidal behaviour. The stress–predisposition model probably has most validity, with long standing issues increasing the vulnerability to suicidal behaviour and more immediate stressors acting as precipitants.

Predisposing factors include genetic and biochemical tendencies, personality traits and the presence or absence of interpersonal support systems. Stressors or triggers include mental disorders, physical illness and alcohol and/or other substance abuse. Almost always there is also a final interpersonal loss or rejection.

Understanding the interaction of possible contributing factors can be a major challenge, as is illustrated by considering various hypotheses to account for the four to one preponderance of males to females committing suicide, and the fact that the highest suicide rates are now in males aged 25 to 44 years, rather than the elderly (Table 1).

Suicide in younger males

The high rates of suicide in younger men may be related to:

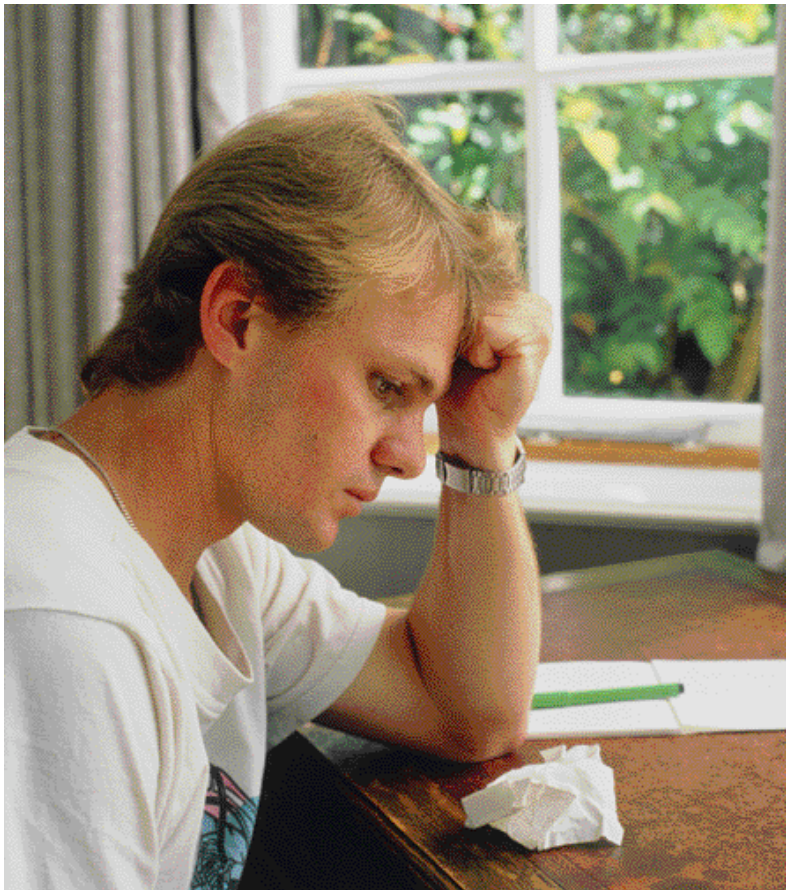
- social changes that provide reduced role

IN SUMMARY

- **Between 2000 and 2500 people die by suicide each year in Australia.**
- **Over 90% of suicides are associated with mental disorders.**
- **There is now persuasive evidence for the effectiveness of both nonpharmacological and pharmacological treatments in reducing suicidal behaviours.**
- **There was a reduction of about 20% in the number of suicides in Australia between the years 1997 and 2003, probably due to better recognition and treatment of mental disorders by GPs.**
- **Continuing vigilance in the detection and management of mental disorders should reduce the number of suicides further.**
- **More males than females commit suicide, and the highest suicide rates are now in males aged 25 to 44 years, rather than in elderly males.**

opportunities, not merely reduced employment options
- alcohol and other substance abuse being particularly prevalent in younger men
- the tendency of younger men to choose the more lethal methods of suicide (such as hanging and carbon monoxide poisoning from car exhaust fumes)
- the Australian macho image, which makes younger men reluctant to acknowledge emotional distress and seek help
- deinstitutionalisation being perceived as the community not wishing to provide asylum and care for people who are emotionally distressed
- media influences resulting in suicide being regarded more readily as an option
- increases in family breakdown.

However, it is not clear why some of these issues would impact more on younger men than on younger women.



PHOTOLIBRARY

Suicide in the elderly

The decrease in the rates of suicide in the older age groups since 1997 may be related to:
- better social security benefits
- more ready acknowledgement of mental disorders, particularly depression, among

Table 1. Suicide numbers and rates in Australia, by age and sex[1]

Age (years)	Number of suicides (age-specific rate, per 100,000)					
	Male			Female		
	1990	1997	2003*	1990	1997	2003*
15 to 24	379 (27.0)	416 (30.6)	251 (18.0)	60 (4.4)	93 (7.1)	49 (3.7)
25 to 34	412 (29.1)	540 (37.5)	407 (28.3)	98 (7.0)	115 (8.0)	111 (7.7)
35 to 44	330 (25.4)	431 (30.2)	381 (25.6)	75 (5.9)	122 (8.5)	102 (6.8)
45 to 54	198 (21.4)	294 (24.4)	299 (22.1)	60 (6.8)	96 (8.2)	93 (6.8)
55 to 64	182 (24.8)	177 (22.6)	154 (15.0)	45 (6.2)	66 (7.2)	59 (5.9)
65 to 74	139 (26.1)	146 (23.6)	128 (19.4)	49 (7.9)	47 (6.9)	33 (4.7)
75+	89 (32.1)	131 (36.2)	109 (22.9)	39 (8.4)	41 (7.0)	23 (3.2)
Total	1735 (20.7)	2146 (23.5)	1736 (17.7)	426 (4.9)	577 (6.1)	477 (4.7)

* Latest figures available.

Table 2. Suicide risk factors

- Depression, particularly with psychotic features
- Previous suicide attempts
- Alcohol and/or other substance dependence
- Schizophrenia
- Hopelessness, despair, guilt, self-absorption
- Malignant alienation
- Chronic physical illness
- Family history of suicide
- Male sex
- Living alone
- Indigenous group
- Custody or prison
- Sexual identity issues

older age groups
- provision of better psychiatric services, including specialised psychogeriatric units
- better treatment of physical illnesses associated with suicide
- improved palliative care
- the possibility that more doctors are now tacitly in favour of euthanasia or death with dignity, so that fewer older people feel the need to take their own lives.

Suicide risk indicators

Although there is no simple cause of suicide, this should not be daunting in the clinical setting. There are clear options for the clinician who is confronted with a suicidal person.

Risk factors for suicide

Broad sociological issues impose their own risks of suicide, but from the clinician's point of view the primary risk factor for all suicidal behaviour is mental illness. Several psychological autopsy studies involving detailed retrospective inquiry have revealed that over 90% of people in the studies who had died by suicide had a potentially recognisable and treatable psychiatric illness.

Depression is the most important clinical syndrome in people who are suicidal, being present in 50 to 70% of all those who suicide (including adolescents, in whom its significance has sometimes been minimised). Schizophrenia and substance dependence are also associated with suicide, as are other factors (Table 2).

The suicidal mind

Suicidal behaviour is a personal phenomenon. Each suicidal person has his or her own view of the world, which frequently becomes constricted so that alternatives to suicide appear remote. The final act is often precipitated by loss of an interpersonal relationship, and fantasies of retribution or retaliation may be present. These feelings sometimes seem to be turned in on the self, so much so that suicide has been referred to as a murder in the 180th degree.

Coupled with feelings of retaliation and retribution on the suicidal person's part, there is often a sense of omnipotence that suicide is not only the solution to his or her problems but also the ultimate method of making others feel sorry for actual or imagined acts against him or her. Other fantasies may be of reunion with significant others who have died, particularly if their death was by suicide.

Clinical warning signs

There are several clinical features that should alert the clinician to the possibility of suicide. The expression of suicidal intent, with depression, agitation, guilt, hopelessness and a constriction of interest or self-absorption, are particularly ominous. So too is malignant alienation, a syndrome seen in those who have exhausted the patience and resources of friends and relatives and also of the helping professions. The person may have been subjected to disparaging comments from others, including clinicians.

Although these factors are associated with suicide risk, the dilemma is that they lack specificity and are of limited value in individual cases. GPs will frequently see patients with these risk factors but suicide is relatively infrequent, although dramatic when it does occur. On average, a GP probably has first hand experience of only one suicide every five years.

Initial management

The fundamentals of managing a suicidal patient are summarised in Table 3.

First contact

The initial contact with a suicidal person is particularly important, but it often occurs in less than ideal circumstances, such as in the home or in a busy emergency room. There may be concerns about the physical condition of the patient and he or she may be antagonistic towards others, including clinicians, as almost invariably the suicidal behaviour will have been precipitated by perceived rejection by someone significant.

Considerable expertise and patience may be required to establish rapport. This may be achieved by emphasising that you want to try to understand what has happened and that a certain amount of time has been set aside to discuss this. It is best to avoid challenging, closed questions such as 'Do/did you really want to die?'. Open-ended enquiry such as 'What are/were your feelings about living and dying?' is far more likely to elicit useful information.

The patient should be given the opportunity to express his or her thoughts and feelings and encouraged and permitted to discharge pent-up and repressed feelings. This catharsis should put the person's suicidal intentions at least temporarily on hold.

It is important to provide the patient with privacy. It is unrealistic to expect someone to divulge sensitive personal

information unless confidentially is assured.

Suicidal intent

It is crucial to consider the degree of suicidal intent, both from the patient's subjective experience and from the clinician's objective assessment. This can be estimated by exploring the following:

- degree of planning
- knowledge of lethality of method
- degree of premeditation
- isolation
- timing
- precautions against discovery
- awareness of chance of rescue
- communication of suicidal ideation
- purpose of attempt
- ambivalence regarding life or death
- presence and content of suicide note
- acts in anticipation of death.

Firearms and other weapons

It is important to ask about the availability of methods for suicide. This may result in the need to invoke local laws about the possession of firearms because the law in most States and Territories mandates that if doctors have reasonable grounds for concern, notification to firearms regulatory authorities is required. Tact is required, and the clinician should emphasis the concern for safety rather than punitive action.

Hospitalisation

Hospitalisation may be necessary for profoundly suicidal people who have a psychiatric illness. Compulsory admission may be required to reduce the risk to the patient or others. In these circumstances it is important to emphasise to the suicidal person and his or her relatives and friends that this is to protect the person, not to punish him or her.

Hospitalisation, or at least specialist psychiatric referral, is advisable if:

- there are specific suicide plans, particularly with associated impulsivity
- an active psychotic illness is present
- there is profound hopelessness and nihilism.

The degree of social support a patient has may also influence the decision to hospitalise.

Subsequent management

The opportunity to express their thoughts and feelings, with resultant catharsis, may be sufficient for some suicidal patients. If there is no psychiatric illness and the suicidal thoughts and actions have resulted in positive changes in personal relationships, further contact may not be necessary. However, the opportunity for follow up should be left open, particularly if there are inadequate social supports.

Psychotherapy

Few people require the support of a therapist for longer than two to three months. This may involve three to six therapy sessions, each of sufficient duration to allow the patient to address their interpersonal difficulties. Cognitive behavioural therapy (CBT) has been demonstrated to be the most effective form of intervention.

Cognitive behavioural therapy

CBT focuses on the here-and-now issues in a problem solving manner. It is based on the fact that most suicidal patients see themselves as inadequate and unworthy, viewing the future with negative expectancies, and anticipating that any initiatives are doomed from the start.

CBT is designed to counteract errors of cognition by asking patients to define specific thoughts that seem plausible to them. The patient's statement is examined objectively in a nonjudgmental manner, and the therapist helps the patient to appreciate that his or her thinking is idiosyncratic and self-defeating. The patient is then invited to generate alternative hypotheses that fit the situation. This important part of the therapy provides the patient with alternative modes of thinking that are less self-defeating and less likely to lead to suicidal behaviour. Indeed, it is useful to insist that the patient clearly describes his or her options, other than suicidal behaviour, should he or she find himself or herself in a similar crisis in the future.

It is sometimes beneficial to involve significant others, such as the person's parent(s), partner or children, because the presence of a neutral therapist allows the expression of mixed feelings in a controlled manner, and further reality testing of behaviour and its effect on others can be explored.

Supportive therapy

Therapists must be willing to listen to the demands of suicidal patients, but these demands cannot be met unconditionally and the focus must be on the person accepting responsibility for his or her own actions. There is a fine line between

Table 3. Fundamentals of management

- Establish rapport
- Assess suicidal intent
- Assess mental state
- Ensure safety
- If no psychiatric illness:
  - catharsis
  - follow up
- If family/interpersonal issues:
  - catharsis
  - CBT/problem solving approach
  - possible referral to social worker or psychologist
- If psychiatric illness:
  - catharsis
  - standard treatment, i.e. CBT/ problem solving approach, with or without psychotropic medication
  - referral to psychiatrist if concerns about diagnosis, illness is severe or no response to initial management

fostering independence and appearing to reject those who are suicidal. The fostering of independence can be aided by the therapist making it quite clear to the patient that his or her involvement will be time-limited and then, at the end of that time, expressing confidence in the patient's ability to cope in a more adaptive manner when future crises arise, even though the person may not be completely at ease with himself or herself.

While this approach is appropriate for most suicidal patients, some – such as young parents with few family and social supports and patients with borderline personalities and chronic psychiatric illness – will require longer term treatment and continuing support from the GP or social agencies.

Pharmacotherapy

There is always concern about prescribing drugs to patients who are suicidal because they might be used in a suicide attempt. However, antidepressant, antianxiety or antipsychotic medications may be prescribed when the signs and symptoms of psychiatric illness warrant their use.

The most commonly prescribed medications are antidepressants. These are particularly useful for patients with the classic biological features of depression, including agitation, poor concentration, insomnia and weight loss.

There has been concern about reports of suicidal behaviour being precipitated by the newer antidepressants. However, recent comprehensive reviews have indicated that there is no adverse association with suicidal ideation or suicide, although there is a weak association (about one in 700 patients) with nonfatal deliberate self-harm, which needs to be balanced with the potential benefits of treating and also the risks of not treating those who are suicidal. It is also apparent that this association is not specific to the newer antidepressants, with similar effects being found with tricyclic antidepressants. The jury is still out as to whether this is an idiosyncratic response or whether it is related to the natural history of improvement from depression, as it has been observed for almost 200 years that the risk of suicidal behaviour persists during early convalescence.

When antidepressants are used, it is imperative that an adequate dose be prescribed. It is also essential to be aware of the potential risk of suicide and the toxicity of the antidepressant used. Newer antidepressants should be prescribed because they are less toxic in overdose. It is also important that the duration of treatment is adequate. Antidepressants should be used for four to six months in patients with a first episode of major depression, for 18 to 24 months in those with a second episode, and long term on a maintenance basis in those who have had three or more episodes.

If compliance is an issue, consideration should be given to using treatment or Guardianship Board orders appropriate to the local community. By the time such approaches are necessary, community mental health workers are likely to be involved. However, it is still important for each patient to have a GP who co-ordinates overall management, particularly in this era of deinstitutionalisation. The GP is in a good position to provide continuity of care, which seems to be at a premium in some public health systems.

Conclusion

GPs should not feel obliged to continue the management of patients who are suicidal. However, they should all possess the clinical skills to make a general assessment and management plan, albeit with referral to a colleague with a specific interest in psychosocial conditions or to a psychologist or psychiatrist. Whereas in the past there was a sense of pessimism about our capacity to prevent suicidal behaviour, now there is sound evidence for the effectiveness of standard treatments for psychiatric conditions that are antecedents of suicidal behaviour.

There has been a reduction in the total number of suicides in Australia over the years 1997 to 2003 and there is no reason to think that it cannot be reduced further, primarily by improved general practice care. MT

Reference

1. Australian Bureau of Statistics. Suicides: recent trends, Australia 1993 to 2003. Canberra: Commonwealth Government; 2004.

Further reading

1. Goldney R.D. Suicide prevention: a pragmatic review of recent studies. Crisis 2005; 26: 128-140.

DECLARATION OF INTEREST: Professor Goldney has received research funding and has accepted honoraria for participating in educational programs from several pharmaceutical companies.

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Reuptake inhibitors for depression

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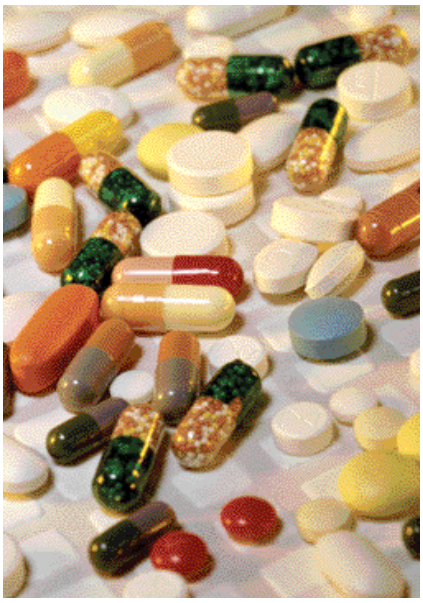
Most of the currently available antidepressants are monoamine neurotransmitter reuptake inhibitors. The development of drugs that are selective for either serotonin or noradrenaline, or both, has resulted in medications with better side effect profiles and reduced toxicity compared with the nonselective reuptake inhibitors, the tricyclic antidepressants.



The management of depression advanced greatly with the development of antidepressant agents based on neurotransmitter reuptake inhibition and, more recently, the development of reuptake inhibitors selective for specific neurotransmitters. These newer antidepressants have fewer side effects and less toxicity than the older agents. The pharmacology of the reuptake inhibitors, and particularly the newer drugs, is discussed in this article.

What are reuptake inhibitors?

Reuptake inhibitors are a group of drugs from several different classes whose mode of action involves blocking the reuptake of monoamine or other types of neurotransmitters from the synapse into the presynaptic neurone. The end effect is an increased synaptic concentration of neurotransmitter. The 'neurotransmitter hypothesis' of depression – that a deficit in monoamine neurotransmitter, notably noradrenaline and serotonin but also dopamine, underlies depression – infers that this increased concentration of synaptic monoamine neurotransmitter is responsible for the antidepressant effect. However, it is clear that this is not an adequate explanation for the antidepressant effect and that other mechanisms such as pre- and postsynaptic receptor effects and postsynaptic intracellular systems are also involved. Moreover, there are monoamine reuptake inhibitors that do not have antidepressant activity (for example, the weight reduction agent sibutramine).

Classes of reuptake inhibitors

Most of the currently available antidepressants are reuptake inhibitors. The exceptions are the reversible and irreversible monoamine oxidase inhibitors (MAOIs; which inhibit the metabolism of monoamines) and the tetracyclic antidepressant mianserin and its analogue mirtazapine (which act by blocking presynaptic inhibitory receptors, thereby increasing the release of noradrenaline in the case of mianserin, and noradrenaline and serotonin in the case of mirtazapine).

Tricyclic antidepressants (TCAs) were the first antidepressants available that inhibited monoamine reuptake, and they are still widely used. They inhibit the reuptake of both serotonin and noradrenaline, but because they also interact with other postsynaptic receptors they are associated with considerable side effects and toxicity. The development of TCA-like drugs that are selective for either serotonin or noradrenaline, or both, has resulted in medications with better side effect profiles and reduced toxicity.

The selective reuptake inhibitors are classified as follows:

- selective serotonin reuptake inhibitors (SSRIs) – citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, sertraline
- serotonin and noradrenaline reuptake inhibitors (SNRIs) – venlafaxine
- noradrenaline reuptake inhibitors (NARIs) – reboxetine.

Bupropion is a dopamine reuptake inhibitor and has antidepressant activity but is approved in Australia only for aiding smoking cessation (the mechanism by which it does this is unclear).

When are reuptake inhibitors used?

Reuptake inhibitors are indicated for the treatment of moderate to severe depression in adults, usually in conjunction with appropriate psychological management. Some of the SSRIs and SNRIs are also approved for the treatment of a variety of anxiety disorders in adults, such as generalised anxiety disorder, panic disorder, obsessive compulsive disorder and social phobia, and for premenstrual dysphoric disorder and post-traumatic stress disorder. There is evidence for the efficacy of

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some SSRIs for the treatment of bulimia. No antidepressants are approved for the treatment of depression or anxiety in children and adolescents. The reuptake inhibitors available in Australia and their Therapeutic Goods Administration (TGA)-approved indications for use are listed in Table 1.

Table 1. Reuptake inhibitors available in Australia[1]

Reuptake inhibitor	TGA approved indications
SSRIs	
Citalopram (Celapram, Ciazil, Cipramil, Talam, Talohexal)	Major depression
Escitalopram (Lexapro)	Major depression; social anxiety disorder (social phobia), generalised anxiety disorder
Fluoxetine (Auscap, Fluohexal, Fluoxebelle, Lovan, Prozac, Zactin)	Major depression; obsessive compulsive disorder; premenstrual dysphoric disorder
Fluvoxamine (Faverin, Luvox, Movox, Voxam)	Major depression in adults; obsessive compulsive disorder in adults, adolescents and children 8 years
Paroxetine (Aropax, Oxetine, Paxtine)	Major depression; obsessive compulsive disorder; panic disorder; social anxiety disorder/ social phobia; generalised anxiety disorder; post-traumatic stress disorder
Sertraline (Concorz, Eleva, Xydep, Zoloft)	Major depression; panic disorder; social phobia (social anxiety disorder) in adults; obsessive compulsive disorder in adults and children 6 years; premenstrual dysphoric disorder
SNRIs	
Venlafaxine (Efexor, Efexor-XR)	Major depression; and also for extended release formulation (Efexor-XR), generalised anxiety disorder, social anxiety disorder, panic disorder
NARI	
Reboxetine (Edronax)	Major depression
TCAs	
Amitriptyline (Endep, Tryptanol)	Major depression; nocturnal enuresis
Clomipramine (Anafranil, Placil)	Major depression; obsessive compulsive disorders and phobias in adults; cataplexy associated with narcolepsy
Dothiepin (Dothep, Prothiaden)	Major depression
Doxepin (Deptran, Sinequan)	Major depression
Imipramine (Tofranil)	Major depression; nocturnal enuresis in children >5 years
Nortriptyline (Allegron)	Major depression
Trimipramine (Surmontil)	Major depression

How are they used?

TCAs as a rule have a linear dose response and therefore they can sometimes be more effective in high doses. However, safety and cardiotoxicity then need careful monitoring and specialist supervision is important.

For SSRIs in general, the starting dose is the therapeutic dose and dosage titration is often not necessary. SSRIs have a relatively flat dose–response curve, meaning that increasing the dose beyond the recommended range is unlikely to increase efficacy for most patients. High doses, however, can be necessary for the treatment of obsessive compulsive disorder.

SNRIs have more of a linear dose response than SSRIs, and titration upwards can usually be expected to increase the response rate. Venlafaxine exhibits mostly serotonergic activity at low to moderate doses and only has significant noradrenergic activity in high doses, so it is only at high doses that it acts as an SNRI.

To lessen initial side effects and improve tolerance, it may be helpful to start any antidepressant with a low dose and then increase the dose gradually. For elderly patients, initial doses should be low and care should be taken to avoid excessively high doses.

Dosing guidelines for the newer reuptake inhibitors are given in Table 2. Once daily dosing is appropriate for most reuptake inhibitors, although dividing the dose sometimes improves tolerance. Morning dosing is suitable for most patients and can prevent excessive night-time stimulation and insomnia, although many patients are comfortable with evening dosing. Reboxetine and the immediate release formulation of venlafaxine are given twice daily.

What needs monitoring?

With all reuptake inhibitors, it is important to monitor symptoms and clinical progress as well as side effects and compliance. In more severe cases, careful monitoring for suicidal thoughts or behaviour is necessary; the first two weeks after starting

treatment for depression is the period of greatest risk for suicide.

In the elderly, monitoring for confusion/delirium and hyponatraemia is prudent.

What are the common side effects?

The common side effects of the SSRIs and SNRIs include nausea, headache, agitation, insomnia, increased sweating and sexual dysfunction (anorgasmia, decreased libido). Less common but important side effects with these inhibitors are bruxism (tooth grinding), myoclonic jerks and subtle cognitive effects such as 'apathy syndrome' and impaired concentration. The NARI reboxetine is associated with anxiety, agitation, insomnia and urinary hesitancy or retention.

The side effects tend to be dose related and often will settle to an acceptable level over one to two weeks; some, however, can be persistent and poorly tolerated. Switching to an alternative drug in the same class may be useful to manage side effects, as not all reuptake inhibitors have the same side effects in a particular individual. Occasionally, patients will have immediate and severe agitation due to excessive serotonin sensitivity, and will be unable to tolerate any serotonergic drug.

Insomnia can be successfully managed with simple sleep hygiene, but the temporary addition of a hypnotic may be necessary. The addition of a sedating antidepressant to treat SSRI-induced insomnia is not appropriate because of the risks of drug interactions and serotonin syndrome (see below).

What are the important interactions and precautions?

Drug interactions

There are important potential drug interactions between SSRIs and other medications because of either the inhibitory effects of SSRIs on liver (cytochrome P450) enzymes or the risk of the serotonin syndrome. Prescribers need to be familiar with the more important and clinically relevant of these. For example, SSRIs will inhibit the metabolism of TCAs, leading to increased serum levels and potential tricyclic toxicity.

SSRIs should not be prescribed concurrently with tricyclics, MAOIs or other serotonergic compounds such as SNRIs, mirtazapine, clomipramine, hypericum (St John's wort) and tramadol because of the risk of serotonin syndrome. (The serotonin syndrome is characterised by changes in mental status and motor and autonomic function. It most commonly occurs as the result of two or more drugs that enhance serotonergic neurotransmission by different mechanisms being administered in combination or taken in overdose, although it may rarely occur

Table 2. The newer reuptake inhibitors: dosing guidelines

Drug	Initial dose	Recommended dose range	Comment
SSRIs			
Citalopram	20 mg once daily	20 to 60 mg/day	–
Escitalopram	10 mg once daily	10 to 20 mg/day	–
Fluoxetine	20 mg once daily (morning)	20 to 60 mg/day (in two divided doses, morning and noon, if >20 mg/day)	Use up to 80 mg for obsessive compulsive disorder
Fluvoxamine	50 mg once daily (evening)	50 to 300 mg/day (in two or three divided doses if >150 mg/day)	–
Paroxetine	20 mg once daily	20 to 60 mg/day	Use upper dose range for anxiety disorders
Sertraline	50 mg once daily	50 to 200 mg/day	–
SNRI			
Venlafaxine	Immediate release formulation, 37.5 mg twice daily; extended release formulation, 75 mg once daily	Immediate release formulation, 75 to 375 mg/day; extended release formulation, 75 to 225 mg/day	–
NARI			
Reboxetine	4 mg twice daily	8 to 10 mg/day	Halve starting dose and dose range in the elderly and in patients with renal and/or hepatic impairment

following overdose of a single agent.)

When changing from one antidepressant to another it is important to observe the recommended washout period to avoid drug interactions.

Precautions

A withdrawal syndrome can occur with the abrupt cessation of any antidepressant and a tapered withdrawal is always necessary. This is particularly important for the serotonergic antidepressants (SSRIs, SNRIs and mirtazapine). Paroxetine and venlafaxine have been associated with particularly prominent discontinuation symptoms and the tapered withdrawal may need to extend over several weeks to minimise discomfort. Common withdrawal symptoms include dizziness, a light-headed feeling, irritability, general malaise and insomnia.

Recently, concerns have been raised about the possible connection between certain SSRIs and the development of suicidal thoughts and behaviour, particularly in adolescents. While further research is needed, there is sufficient concern to recommend careful monitoring for the emergence or worsening of suicidal thoughts during the initial two to three weeks after commencing any antidepressant.

Conclusion

Antidepressants are believed to exert their therapeutic effect by increasing the synaptic concentration of neurotransmitters, principally noradrenaline and serotonin. Reuptake inhibition is one mechanism by which this can be achieved. The newer reuptake inhibitors, because of their greater selectivity, have significant advantages in safety and side effects compared with the original reuptake inhibitors, the tricyclics. The successful treatment of the more severe forms of depression will usually involve antidepressant medication. An understanding of the mechanisms of action of the various antidepressants will assist the clinician in appropriate drug selection for the individual patient. MT

Reference

1. MIMS Australia. Issue No. 1 2006 (February/March). Sydney: CMPMedica Australia.

DECLARATION OF INTEREST: Dr Lyndon serves on advisory boards for Eli Lilly, Lundbeck and Synofi-Synthelabo and is involved in industry sponsored clinical trials for AstraZeneca and GlaxoSmithKline. He frequently delivers industry sponsored lectures and educational symposia and has been sponsored by various pharmaceutical companies to attend overseas meetings. He is a member of the organising committees for several annual psychiatric conferences sponsored by various pharmaceutical companies.