Depressive disorders are more common in patients with physical illness than in those without, with up to one-third of medical in-patients reporting mild to moderate symptoms of depression (Rodin & Voshart, 1986). Some medical conditions have a stronger association with psychiatric illness than others, for example the prevalence rates of depressive illness in patients with diabetes, cardiac or neurological disease is about 25%, but not much more than the general population in those with hypertension. Medical in-patients are more likely to have depression than are out-patients. There are a number of potential factors that may contribute to this increased risk of depression in people with physical illness, as outlined in Box 1.

Despite this increased prevalence, there has been widespread neglect of depression in patients with medical disease (Royal College of Physicians & Royal College of Psychiatrists, 1995), contributing to a number of poor outcomes. Physical problems are underdiagnosed in psychiatric patients. Patients with physical illness and depression have poorer levels of functioning and higher levels of mortality and morbidity compared with patients with similar illnesses but without depression (Wulsin et al, 1999).

Physicians may assume that the medical illness caused the depression, or is a contraindication to antidepressant drug treatment. Medical patients with depression use more medical health care resources than those without, both for assessment and treatment – for example, the frequency of a patient’s attendance at a medical out-patient clinic is better predicted by how depressed he or she is than by his or her underlying medical condition. This contrasts with evidence of good outcomes in patients who do receive appropriate treatment, including relief of psychological distress, improved rehabilitation potential (following a stroke or myocardial infarct) and reduced health care costs.

This article outlines the assessment of depression in patients with physical illness, explores some of the diagnostic issues involved and reviews the treatment options available.

Box 1 Factors contributing to the increased risk of depression in physical illness

<table>
<thead>
<tr>
<th>Biological</th>
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<tr>
<td>Hormonal, nutritional, electrolyte or endocrine abnormalities</td>
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<td>Effects of medication</td>
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<tr>
<td>Physical consequences of systemic and/or intracerebral disease</td>
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<table>
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<tr>
<th>Psychological</th>
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<tr>
<td>Sense of loss associated with serious medical illness</td>
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<tr>
<td>Effects on body image, self-esteem, sense of identity</td>
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<tr>
<td>Impaired capacity to work and maintain relationships</td>
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Relationship between depression and physical illness

The comorbidity of depressive and physical illnesses may be understood in a number of different,
potentially overlapping, ways. First, and most commonly, the physical condition causes the depressive illness. This may be owing to a presumed direct biological mechanism, especially if the disease involves the endocrine or central nervous systems. Box 2 gives examples of some of the many drug treatments for physical illness that may have depressive side-effects. In a more comprehensive list, Bazire (2001) notes well over 100 drug treatments reported as causing depressive illness.

The physical condition may also trigger depression via a psychological response, especially if the condition is particularly disfiguring, disabling or potentially fatal. Overall, two-thirds of depressive illness in general medical wards is a direct result of the physical illness or its treatment. Box 3 outlines the factors that increase the likelihood that patients who are physically ill will develop a depressive illness. Of these, the single most important predictor is a previous episode of depression.

Second, the physical problems develop or increase owing to depressive illness. This may range from acute liver failure following paracetamol overdose in a patient with depression to the physical complications of chronic substance misuse. Depressive illness contributes to other alterations in health-related behaviours, including poor compliance with medications, diet, exercise and utilisation of health care services. Dinan (1999) has suggested that the increased risk of coronary artery disease and reduced bone mineral density in patients with depression is caused by increased activation of the hypothalamic–pituitary–adrenal axis causing hypercortisolism.

Third, the depressive and physical illnesses may have a common cause, for example bereavement or stress triggering stroke and depression.

Finally, the depressive illness may be coincidental and unrelated to physical problems, as both physical and psychiatric conditions are common in the general population. Depression pre-dates the medical illness in up to 25% of patients with comorbid depression, and it is associated with an increase in somatic complaints.

**Assessment**

The basic principles of biopsychosocial assessment and management of any patient with a psychiatric disorder apply, with some modification. Patients within the general medical system may be angered or distressed by the recommendation for psychiatric referral. A joint Colleges report on the psychological care of surgical patients (Royal College of Surgeons & Royal College of Psychiatrists, 1997) offers guidance on how to instigate such a referral. Seeing the patient in the setting of the general practitioner’s surgery or a medical hospital is more likely to encourage attendance. Checking that an in-patient has been told of the psychiatric referral before you arrive on the ward can prevent embarrassment for you both.

It is essential to have some understanding of the patient’s physical problems, treatment and prognosis. The relevant issues are better clarified by direct liaison with the medical team, rather than relying on medical documentation alone.

During the introduction, it is important to clarify that you are a psychiatrist and to explore at this point what the patient feels about the referral. This may vary from concerns that they are mad, to relief at having their emotional distress recognised, and the discussion encourages rapport. The initial focus of the assessment from this point should concentrate on the general medical history, before gradually introducing and elaborating on psychological symptoms, as tolerated by the patient.
Diagnosis of depression in physical illness

Depression is more difficult to diagnose in patients with physical illness. The biological symptoms of depression include anorexia, weight loss, sleep disturbance, lethargy and psychomotor retardation, all of which may equally be due to the physical illness. However, the consensus is that it is probably best to apply psychiatric diagnostic criteria without modification, while being aware of the risk of overdiagnosis, so that all symptoms are considered whatever their cause may be. It is particularly important that the assessment focuses on the cognitive symptoms of depression. Somatic symptoms are used to support the diagnosis of major depression if they are severe, disproportionate to the medical illness and temporally related to the affective cognitive symptoms of depression. Hawton et al (1990) reported three cardinal affective symptoms that help to differentiate depression from non-depression in medical patients – depressed mood, morning depression and hopelessness. Inappropriate guilt, feeling punished, lowered self-esteem and suicidal ideation are reported less frequently by patients with depression in a medical rather than a psychiatric setting. However, patients with depression who are also medically ill are more likely to feel anxious, pessimistic and helpless than those who have depression but are physically well.

Covert manifestations of depression include poor compliance or refusal of essential medical treatment. The number of somatic complaints is directly proportional to the likelihood of depressive illness in the medical as well as the psychiatric patient and they may present with abnormal or exaggerated illness behaviour, pain or other somatic symptoms rather than low mood.

Differential diagnosis

It is also important to consider other potential causes of low mood in patients with physical illness. These include the normal and understandable emotional reactions to physical ill health. Adjustment reactions, for example those triggered by the stress of physical illness, are the most common psychiatric diagnosis, affecting approximately one-quarter of general medical patients. Psychological symptoms of depression are common in delirium, particularly quiet or hypoactive delirium, which is often referred as depressive illness for psychiatric assessment (Meagher, 2001). Differentiating between the two conditions is particularly relevant to allow early treatment and avoid potential increased confusion resulting from the anticholinergic side-effects of antidepressant therapy. Substance misuse also needs to be considered as relevant to lowered mood in a number of ways, such as in a patient whose increasing alcohol misuse has resulted in a severe exacerbation of psoriasis. In organic affective disorders such as hypothyroidism, it is important to treat the underlying physical condition appropriately and then to reassess mood before considering antidepressant medication. Finally, a trial of antidepressant therapy may be useful in diagnostic dilemmas.

Rating scales

A number of screening tools, such as the Hospital Anxiety and Depression Scale (Zigmond & Snaith, 1983), have been specifically developed for use in the general hospital setting. The Beck Depression Inventory (Beck et al, 1961) has been helpful, given its emphasis on cognitive symptoms, for example in assessing depression in patients with multiple sclerosis. However, a recent systematic review looking at the usefulness of routinely administered psychiatric questionnaires in non-psychiatric settings concluded that it was a costly exercise that did not influence clinicians’ behaviour (Gilbody et al, 2001). Such screening tools cannot replace thorough clinical examination of individual patients.

Assessment of capacity and the Mental Health Act

Occasionally the psychiatrist will be called to assess capacity in a patient with depression who is refusing treatment. All adults are presumed to have capacity unless it is proved otherwise. Capacity is considered present if the patient can comprehend, retain and believe the information about the treatment, and if he or she weighs that information in arriving at his or her decision. It is considered to be task-specific, with greater capacity required for more important decisions, such as discontinuation of renal dialysis. In Scotland, the medical treatment section of the Adults with Incapacity (Scotland) Act awaits imminent introduction. This will be relevant for any non-emergency medical intervention. All emergency treatments will still be covered by common law.

The Mental Health Act 1983 allows the legal detention of patients who meet the necessary criteria of mental disorder, require hospital admission and are unwilling to enter or stay in hospital. These
issues often require clarification with medical and general nursing colleagues, who may erroneously believe that the Mental Health Act is required to ensure treatment of a non-compliant patient. Although it is not relevant to the treatment of physical disorder as such, the Mental Health Act may apply where the physical disorder contributes to the mental disorder, such as when using thyroxine to treat mental disorder resulting from hypothyroidism.

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**Treatment of depression in physical illness**

The question of where a patient who has severe depression should be treated depends essentially on the severity of his or her medical condition. If his or her physical condition can only be treated in a medical hospital setting then the medical and nursing staff need to be involved in discussions regarding whereabouts in the hospital (consider transfer to a ground floor ward, for example, balanced against the risk of losing touch with the core medical team), suicide risk, levels of observation required, whether a psychiatric nurse is required and if the patient is detainable. There is an increased risk of suicide in patients who have chronic physical illness and pain. Particular caution is required with elderly patients in this category, who may deny significant suicidal ideation. When writing in the medical records it is best to highlight relevant aetiological factors, diagnosis and the management plan, for purposes of confidentiality. The full psychiatric history can then be confined to psychiatric records.

Again, the treatment approaches that apply are the same as in the case of any patient with depression, but with some modification. This will depend on the cause and severity of the patient’s physical illness and the treatment setting. The biopsychosocial approach is particularly relevant here. As with any patient with depression, treatment should always involve supportive and problem-solving strategies, education, support for family members and opportunities to discuss social difficulties. For hospital in-patients, regular physiotherapy and occupational therapy are essential to help patients cope with boredom, pain and isolation on the ward. Address any contributory factors, such as treatment of any medical cause of the depression. If it is not possible to withdraw a medication contributing to the depressed mood then antidepressant medication should be considered.

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**Psychological treatments**

The main potential benefit of considering a purely psychotherapeutic approach to treatment is the avoidance of drug interactions or side-effects exacerbating the physical problems. However, it is often impracticable owing to expense, lack of availability of skilled therapists, the difficulty in its application in the ward environment or for a patient who has difficulty in travelling, and the fact that it is less acceptable to some patients and their physicians than medication. Guthrie & Creed (1996) note the paucity of evidence for the efficacy of psychological treatment in chronic physical disease. Psychological therapy has been particularly neglected in older patients, who often require longer periods of treatment.

Specific psychological therapies such as problem-solving, cognitive–behavioural therapy (CBT) or interpersonal therapy (IPT) may be used as an alternative or adjunct to antidepressant medication for mild depressive disorders in those with physical illness. Of these, CBT has been the most frequently applied. The intrinsic acknowledgement of physical symptoms within the theoretical framework is particularly useful, and CBT is now well incorporated by health psychologists into cardiac rehabilitation and chronic pain programmes.

There has been recent evidence of the usefulness of psychotherapy for depression in patients with a range of physical illnesses. This includes the study by Lustman et al (1998) of 10 weeks of individual CBT along with supportive diabetic education. The authors concluded that this was an effective treatment for major depression in patients with non-insulin dependent diabetes, and also noted improved hypoglycaemic control. Kunik et al (2001) reported that a brief 2-hour CBT session resulted in a significant reduction of depressive and anxiety symptoms (but no change in physical functioning) in patients with chronic obstructive pulmonary disease, compared with a group that received 2 hours of simple education. In a prospective study, CBT was also reported to have an impact on levels of depression in an unselected group of out-patients with rheumatoid arthritis (Leibing et al, 1999). The beneficial effects of various psychosocial interventions on anxiety and depression in oncology patients have been well described. There have been recent developments in psychooncology, ranging from cognitive–existential group therapy to family grief therapy (Bloch & Kissane, 2000).

White (2001) has recently published a guide on the application of CBT in the treatment of chronic medical problems such as cancer and diabetes and in cardiology and dermatology.
Box 4 Important drug interactions

Reduce and monitor lithium levels if taking non-steroidal anti-inflammatory drugs
Reduce propanolol dose if selective serotonin reuptake inhibitors (SSRIs) have been prescribed
Reduce doses of tricyclic antidepressants (TCAs) or moclobemide if taking cimetidine
Increase dose of TCAs by up to one-third if on a high-fibre diet
Reduce and monitor warfarin dose if fluoxetine or fluvoxamine have been prescribed
Reduce dose of donepezil if an SSRI is added
Avoid monoamine oxidase inhibitors with opioids
Dextropropoxyphene increases carbamazepine (CBZ) levels
Avoid TCAs and CBZ if bone marrow suppression occurs due to chemotherapy
SSRIs/clomipramine and selegiline (Parkinson’s) may trigger acute confusion
Lithium and sumatriptan (migraine) may trigger central nervous system toxicity
TCAs have reduced efficacy and increased toxicity with the oral contraceptive pill

Medication

General issues

Antidepressant medication is cheap and readily available. It should be considered whenever symptoms of depression persist, despite treatment of the underlying medical condition or brief psychotherapeutic interventions. The threshold for prescribing antidepressants is generally higher in this patient group, however, because of the risk of metabolic complications and/or drug interactions. The choice of drug depends on the physical illness of the patient and medications already prescribed, influenced as in usual practice by response to previous treatments. Because of increased sensitivity to side-effects in those with medical illness, treatment may need to be introduced at a lower dose, such as paroxetine 5–10 mg, before cautiously increasing this. Dividing out the dose may also improve tolerance.

Essential prescribing information is published in the British National Formulary (BNF; British Medical Association & Royal Pharmaceutical Society, 2002), which should always be consulted about precautions needed and potential drug interactions. Some important examples of drug interactions are given in Box 4. Other useful references are the Psychotropic Drug Directory (Bazire, 2001) and the Maudsley Prescribing Guidelines (Taylor et al, 2001), which provide more detailed information on psychotropic prescribing in medical conditions. Particular care is required in patients with renal, hepatic, diabetic, neurological and cardiovascular disease, as outlined below. In general, the most important maxims in prescribing for this population are (a) use your BNF and (b) start low and go slow.

Tricyclic antidepressants v. selective serotonin reuptake inhibitors

We have evidence from the Cochrane Collaboration that antidepressants are both effective and acceptable for treatment of depression in patients with physical illness (Gill & Hatcher, 2001). The authors conclude that antidepressant treatment is significantly more likely than placebo to result in clinical improvement in patients with a wide range of physical illness. They also comment on the acceptability of such treatments to patients, with a drop-out rate of about 1 in 10. Trends were noted of tricyclic antidepressants (TCAs) being more effective than selective serotonin reuptake inhibitors (SSRIs), but also more likely to produce drop-outs. The anticholinergic side-effects of the TCAs have been a particular problem for patients with physical illness. However, SSRIs and the other newer antidepressants are not without their disadvantages. Parker (2001) has argued convincingly that SSRIs are less effective in the treatment of melancholic depression than TCAs, with the two groups appearing equally effective in the treatment of non-melancholic depression. A judicious balance of informed clinical judgement, patients’ symptoms, side-effects (wanted and unwanted) and cost helps to direct the choice of antidepressant.

Given the increasing first-line use of SSRIs in this population, it is important to be aware of the differences within groups. These are largely based on their differences in half-life and potential for cytochrome P450 (CP450) inhibition. Anderson & Edwards (2001) have produced useful guidance on how to choose between the individual drugs. For example, compared with other SSRIs, fluoxetine may be more likely to cause dermatological reactions, agitation and weight loss. Its long half-life may also
Venlafaxine may cause hypertension, with blood pressure monitoring recommended at doses above 200 mg daily. Paroxetine, trazodone or nefazodone may be considered if sedation is required, but the patient must be monitored for hypotension. Lithium is known to cause electrocardiogram (ECG) changes, such as flat or inverted T-waves (generally benign), and widened QRS complexes. Hence it should be prescribed cautiously in patients with pre-existing conduction abnormalities. It is contraindicated in cardiac failure and sick sinus syndrome, but otherwise is not a significant risk. A baseline ECG and yearly repeats, as well as routine urea and electrolyte monitoring is essential and, of course, particular caution is required when prescribed along with diuretics.

**Hepatic disease**

All antidepressants are predominantly metabolised by the liver and so have increased half-lives with reduced clearance. The severity of impairment rather than the underlying aetiology is the most important factor to consider in prescribing for this group. Renal function may also be affected. As the risk of drug toxicity increases with disease severity, lower starting and total doses of medication are recommended. Of the SSRIs, paroxetine prescribed at the lower end of the dose range seems to be the safest option. Citalopram in the lower dose range and fluoxetine at half the usual dose, or given on alternate days, will have less sedative effects. Sertraline and lofepramine are to be avoided.

The sedative and constipating side-effects of the TCAs may precipitate or unmask subclinical hepatic encephalopathy. Of the group, imipramine is probably the best, commencing at 10 mg three times daily for 2 weeks, then increased by 10 mg weekly until it is effective. Venlafaxine, nefazodone, mirtazapine and reboxetine should all be started at a low dose with cautious titration. Monoamine oxidase inhibitors (MAOIs) are hepatotoxic and may precipitate coma. If essential, the starting dose should be very low, with moclobemide being the safest option. As lithium undergoes minimal hepatic metabolism, it is the mood stabiliser of choice in liver disease.

**Renal disease**

In this group of patients, TCAs are probably safer than SSRIs. As with hepatic disease, the degree of renal impairment rather than the cause is most important. Renal impairment may be present in the elderly without a raised creatinine level. TCA metabolites are excreted by the kidneys, hence accumulation may occur. Again, start low and go slowly; for example commence amitriptyline at 25 mg/day in divided doses and increase by 25 mg

**Elderly patients**

Caution is advised for all aspects of prescribing for elderly people. For example, they are particularly sensitive to postural hypotension and anticholinergic side-effects from TCAs. SSRIs, moclobemide, trazodone and nefazodone are better options owing to lower cardiac and anticholinergic effects, although half-lives of sertraline and citalopram are prolonged in elderly patients.

**Specific disorders**

**Cardiovascular disease**

Myocardial infarction is associated with an increased incidence of depression, which in turn is associated with increased mortality post-myocardial infarction. It is therefore important to actively instigate treatment, bearing in mind that all antidepressants are best avoided for 2 months after a myocardial infarction, if possible. Usually, the first choice is an SSRI medication, avoiding fluvoxamine and citalopram if there is a risk of overdose, which has been linked to cardiotoxicity. SSRIs may trigger an initial modest slowing of the heart rate, to which the patient usually adapts. TCAs cause orthostatic hypotension and increased heart rate, which may exacerbate angina. Although antiarrhythmic in high doses, their anticholinergic and quinidine-like effects can trigger cardiac arrhythmias, and are only prescribed in patients with severe conduction defects if they have pacemaker cover. A recent case-control study has reported a dose-related increased risk of ischaemic heart disease in patients who had ever taken dothiepin but not other TCAs (Hippisley-Cox et al, 2001). Of the newer antidepressants, mirtazapine seems safe for patients with arrhythmias. Venlafaxine may cause hypertension, with blood pressure monitoring recommended at doses above 200 mg daily. Paroxetine, trazodone or nefazodone may be considered if sedation is required, but the patient must be monitored for hypotension. Lithium is known to cause electrocardiogram (ECG) changes, such as flat or inverted T-waves (generally benign), and widened QRS complexes. Hence it should be prescribed cautiously in patients with pre-existing conduction abnormalities. It is contraindicated in cardiac failure and sick sinus syndrome, but otherwise is not a significant risk. A baseline ECG and yearly repeats, as well as routine urea and electrolyte monitoring is essential and, of course, particular caution is required when prescribed along with diuretics.

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weekly as tolerated. Avoid lofepramine because much of it is excreted, unchanged, by the kidneys.

Of the SSRIs, sertraline is not recommended by its manufacturers in renal failure. Fluoxetine, citalopram and paroxetine should be started at 10 mg daily (or 20 mg alternate days in the case of fluoxetine) in patients with a glomerulofiltration rate of at least >10 ml/min. Carbamazepine and valproate are the preferred mood stabilisers in renal failure. Lithium should only be prescribed if absolutely necessary, at low doses, on alternate days, with frequent checking of serum levels.

**Diabetes mellitus**

Selective serotonin reuptake inhibitors may reduce serum glucose by up to 30% and cause appetite suppression, resulting in weight loss. Fluoxetine should be avoided, owing to its increased potential for hypoglycaemia, particularly in non-insulin dependent diabetes. Its side-effects of tremor, nausea, sweating and anxiety may also be misinterpreted as due to hypoglycaemia (Bazire, 2001). If fluoxetine is prescribed, the patient should be advised of the need to monitor serum glucose levels regularly. TCAs are more likely to impair diabetic control as they increase serum glucose levels by up to 150%, increase appetite (particularly carbohydrate craving) and reduce the metabolic rate. They are generally considered safe unless the diabetes is very poorly controlled or is associated with significant cardiac or renal disease. Antidepressants such as amitriptyline, imipramine and citalopram are also used to treat painful diabetic neuropathy. Of the mood stabilisers, lithium can be used safely in patients without renal disease. Sodium valproate may give false positive urine tests (for glucose) in patients with diabetes.

**Neurological disorders**

In patients with epilepsy, all non-MAOIs may lower the seizure threshold. This applies to the TCAs more so than the SSRIs, which are generally the first choice. A slow rate of introduction reduces the risk of a seizure. Of the TCAs, doxepin is considered less and amitriptyline more epileptogenic. The manufacturer recommends avoidance of all MAOIs other than moclobemide while on carbamazepine. Lithium is very epileptogenic in overdose but otherwise this is not a problem at treatment doses.

Depression is common in patients with multiple sclerosis. It may be triggered by drug treatments such as interferon β, adrenocorticotropic hormone or steroid therapy, in which case a reduction or withdrawal of the medication should be considered. Although the TCAs are effective, they are poorly tolerated owing to side-effects, including increased hypertonicity and spams. The SSRIs are therefore the first choice for these patients.

Depression has been reported as more common in vascular than Alzheimer’s dementia, unrelated to the level of cognitive impairment, and occurring at any stage of dementia. The presentation will often be atypical and should be considered for patients showing a sustained change of behaviour. Tune (1998) recommends the use of SSRIs with a potentially stimulant effect such as fluoxetine and sertraline. There is some evidence of donepezil having an antidepressant effect. As donepezil is metabolised by CP450 isoenzyme inhibitors, it should be used with caution in patients on SSRIs.

The amotivational syndrome of Parkinson’s disease may be difficult to distinguish from depressive illness, and the additional symptom of anhedonia is helpful in differentiating the two. TCAs are effective and their anticholinergic effects may help extrapyramidal symptoms (EPS), but potentially increase confusion. SSRIs may exacerbate tremor and should not be prescribed for patients on selegiline (an MAO-B inhibitor), owing to serotoninergic reactions and increased EPS. Clomipramine and MAOIs should similarly be avoided with selegiline. Carbamazepine is the preferred mood stabiliser as lithium and valproate may exacerbate tremor.

Antidepressant choice after stroke depends on the patient’s age, epileptic potential and medications, which will often include anticoagulants or cardiac treatments. SSRIs are the drugs of choice. TCAs again are poorly tolerated owing to anticoagulants or cardiac side-effects, epileptogenicity and cardiac side-effects. Of the group, nortriptyline seems to be the best tolerated and has been used effectively to treat post-stroke depression. Trazodone and nefazodone have less cardiac and anticholinergic side-effects and may be useful alternatives. Potential interactions may occur with aspirin, which increases the free plasma concentration of highly protein-bound drugs such as fluoxetine, paroxetine, sertraline and valproate. Citalopram is the least likely of the SSRIs to interact with warfarin.

**Electroconvulsive therapy**

The American Psychiatric Association Task Force’s report on electroconvulsive therapy (ECT) (American Psychiatric Association, 1990) cites no absolute contraindications to ECT. With continuing advances in the use of ECT it is now used relatively safely in cardiac, pregnant and elderly patients. However, it is wise to proceed particularly cautiously in patients with increased intracranial pressure, a recent intracranial bleed or myocardial infarction, cerebral or aortic aneurysms, acute respiratory tract infection and patients at risk of complications from a general anaesthetic.
Conclusion

As so many of the patients we see have a comorbid physical illness, all psychiatrists need to be proficient in the management of depression in physical illness. Recent advances in psychiatric treatments, including brief focused psychological therapies and increasingly selective medications, have now given us the opportunity to make a significant impact on the health of this previously neglected patient group.

References


Multiple choice questions

1. The following may be signs of depressive illness in a medical patient:
   a refusal of renal dialysis  
b abnormal illness behaviour  
c poor compliance with medical treatment  
d hypoactive delirium  
e multiple somatic symptoms.

2. Depressive illness is more likely in:
   a medical out-patients than in-patients  
b patients with a past psychiatric history  
c patients with disfiguring illnesses  
d patients with hypertension  
e patients who have multiple sclerosis.

3. The following symptoms are particularly useful in helping to diagnose depression in physical illness:
   a depressed mood  
b sleep disturbance  
c hopelessness  
d psychomotor retardation  
e morning depression.

4. The SSRIs are usually the drugs of first choice in the following conditions:
   a cardiovascular disease  
b hepatic disease  
c renal disease  
d neurological disorders  
e patients with a history of gastrointestinal bleeding.
5. The following statements regarding the treatment of depression in patients with diabetes are correct:
   a. fluoxetine is the preferred drug treatment
   b. TCAs may cause hypoglycaemic episodes
   c. TCAs should be avoided even if the diabetes is well controlled
   d. sodium valproate is the mood stabiliser of choice
   e. citalopram may also be used to treat diabetic neuropathy.

### Commentary

Chris Dickens

As the arsenal of antidepressant drugs increases with time so, concurrently, does the list of caveats that must be considered when using these agents in patients with other physical illnesses and using other medications. MacHale's (2002, this issue) overview of the management of depression in physical illness serves as a crucial update for clinicians providing psychiatric services for patients with comorbid physical illnesses. Appropriate emphasis is placed on the usefulness of non-pharmacological treatments in such patients, although the reality of modern practice is that drug treatment is most often considered first-line owing to limited psychological service resources.

MacHale draws attention to the raised prevalence of depression in physically ill populations, though it is worth emphasising the complexity of this issue. First, estimating the prevalence of depression among subjects with physical illness from the research evidence available is not straightforward owing to the wide ranging methodologies used and the widely varying prevalences obtained. In general, however, a pattern emerges from this disparate literature that indicates that depression occurs in 10–15% of in-patient and out-patient populations on average, that is 2 to 3 times the rates seen in the general population. In addition to these, a similar proportion of patients have an excess of psychological symptoms. The latter group, while not fulfilling diagnostic criteria for a significant psychiatric illness, cannot be neglected because they represent an ‘at-risk population’ with a raised likelihood of developing a depressive disorder in the near future.

Prevalence rates for depression are raised, although not as dramatically, in general practice and hardly raised (if at all) in non-patient, asymptomatic subjects with physical illness (such as hypertension). Conversely, the prevalence of depression is raised further in specialist (tertiary) care settings and in subjects with highest levels of pain and disability, for example patients undergoing medical rehabilitation, with prevalence rates for depressive disorder reaching 50% in some patient groups. This pattern partly reflects an increased risk of depression as the severity of symptoms present increases. This is not the entire story, however.
Patients with physical illness and depression are more likely to worry about physical symptoms, to interpret symptoms catastrophically and to present to their general practitioners. Such patients with depression are less likely to be satisfied with their medical treatment or to comply with any treatment offered. This probably results in these patients with depression being referred on to specialist services more frequently.

The causes of depression in physical illness are complex. In some conditions, the association with depression is strong and assumed to be due to a direct link between pathophysiological processes and depression, for example Parkinson’s disease, stroke, hypothyroidism or medical treatments and depression. In other conditions, depression is often attributed to the burden of chronic symptoms. The link between depression and symptom load is, however, not clear. Certainly, there is a positive correlation between the prevalence of depressive symptoms and the number and severity of physical symptoms. However, this association appears to be weak at best. Convincing evidence of an association between physical illness and depressive disorder becomes apparent only in those who have the most disabling conditions, such as advanced rheumatoid arthritis. Social stresses, either associated with the medical condition or completely independent, appear to be very important aetiological factors for depression, as they are in physically fit patients with depression. Inherent vulnerability to depression and the efficacy of cognitive coping strategies mediate this complex process.

The impact of depression in physical illness is extremely variable. Depression increases the burden of misery, thus further impairing quality of life. In addition to this, however, depression has wider implications for the course and management of the physical illness itself. Depression, when present in association with a physical illness, is linked with a more negative outcome. Mortality rates may be raised: in the 6 months following myocardial infarction, there is a four-fold increase in mortality for patients with depression compared with patients with otherwise similar cardiovascular profiles but who do not have depression. These figures, generalised to the whole of the UK, suggest that depression may contribute to the early deaths of up to 200 000 patients after myocardial infarction.

Furthermore, patients with physical illness and depression are more likely to have further acute episodes of illness, require more hospitalisations and are likely to remain in hospital for a greater duration when they are admitted. As the result of these factors, health care costs for patients with physical illness and depression exceeds those for their counterparts without depression even after controlling for the severity of their illness. In a recent study of general medical in-patients, we found those with depression incurred costs 50% greater than those without depression. Hidden costs are also likely to be much greater for those with both physical illness and depression. Depression increases disability, predicting poorer functional status, more disability days and a delayed return to work following a period of sick leave.

A number of mechanisms have been proposed to explain how and why depression is associated with a more negative physical outcome in physical illness. Depression has been associated with a number of physiological changes that may contribute to this negative outcome, such as changes to the autonomic nervous system and the hypothalamic–pituitary–adrenal axis activity, and impairment in immune function. In addition, depression is associated with a number of adverse health behaviours that are also likely to contribute to an adverse outcome. Patients with depression are less likely to adopt positive health behaviours (diet, etc.), more likely to persist with negative health behaviours (e.g. smoking and excessive alcohol intake) and less likely to comply with treatment (take medication as prescribed, maintain self-monitoring regimes). Patients with physical illness and depression perceive their illness more negatively. They perceive the consequences of their illness as more serious, the likely duration of their symptoms as greater and their ability to control their disease as less adequate.

It is clear that treating depression in physical illness is important not only to optimise mental health but also to improve the outcome of the physical illness itself.

Reference

Managing depression in physical illness
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