Diagnosis and treatment of mood disorders in patients with rheumatic disease

Mood disorders are common among the medically ill and tend to worsen, as illness becomes more severe. Major depressive disorder (MDD) occurs in 4–6% of the general population, in 5–10% of medically ill outpatients, and in 10–30% of hospitalised medical inpatients. Rheumatic diseases such as fibromyalgia, chronic fatigue/pain syndromes, rheumatoid arthritis, systemic lupus erythematosus (SLE), scleroderma, and Sjögren’s syndrome (SS) are associated with psychiatric disorders or symptom states. Depression is associated with increased functional disability, pain, and stressors like low autonomy, low income, marital status and high demands. By nature recurrent and progressive, it should be diagnosed and treated as soon as possible.

Patients with fibromyalgia and chronic fatigue/pain syndromes have premorbid and significantly higher rates of psychiatric disorders than do patients with rheumatoid arthritis, who were found to have similar rates of depression when compared with those with other chronic medical illnesses. In patients with rheumatological disease, SLE is the disease that poses many dilemmas to the treating physician. The diffuse, non-focal neuropsychiatric presentations of affective, behavioural, and cognitive symptoms in patients with SLE may be attributable to one or several neuropsychiatric disorders, occurring sequentially or simultaneously. No matter the origin of the mood disorder, treatment goals for depression include restoration of normal mood, prevention of suicide, return of self esteem, improvement in the quality of life and work productivity, and increase in satisfaction of both patients and doctors.

Diagnostic precision is required to provide timely and appropriate care. An accurate diagnosis of psychiatric disorders is made by the application of specific diagnostic criteria according to the fourth edition of the Diagnostic and statistical manual of mental disorders (DSM-IV) by assessing onset, duration, and course of depression. This is the gold standard of for diagnosing MDD. At least five of the following nine symptoms must be present most of the day, nearly every day for at least two weeks, and must include either depressed mood or loss of interest or pleasure:

- depressed mood
- markedly diminished interest or pleasure in all, or almost all, activities
- significant weight loss or gain
- insomnia or hypersomnia
- psychomotor agitation or retardation
- fatigue or loss of energy
- feelings of worthlessness or excessive inappropriate guilt (may be delusional)
- diminished ability to think or concentrate, or indecisiveness
- recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without plan, or a suicide attempt or a specific plan for committing suicide

In the medically ill, four of these symptoms (sleep disturbance, appetite disturbance, fatigue or energy loss, and difficulty with concentration) could be viewed as attributable to the medical illness rather than attributable to depression. As long as the patient gives a history of either depressed mood for most of the day almost every day or loss of interest or pleasure in almost all activities, these four symptoms should be counted regardless of what may have caused them. This is the inclusive approach used on our consultation service.

There are other approaches to diagnosing depression in the medically ill. The substitutive approach emphasises impaired concentration and indecisiveness rather than loss of energy. The exclusive approach eliminates anorexia and loss of energy from the list of nine symptoms; in addition, it requires five of the seven remaining DSM criteria to diagnose depression in a medically ill patient. Because this approach leads to false-negative results, its sensitivity is poor.

Self administered scales (for example, Beck Depression Inventory, Zung Self-Rating Depression Scale) are helpful in screening for depression and following the improvement of depressive symptoms after starting treatment. Depending on the scale used, rates of mood disorders in rheumatological patients are different. We recommend that the diagnosis should be made by the applications diagnostic criteria using the inclusive approach.

In SLE patients, careful identification of neuropsychiatric phenomena and generation of a differential diagnosis are crucial. Miguel et al made organic diagnoses of depressive symptoms in patients with concomitant lupus and depression. Or et colleagues showed that patients with CNS lupus and secondary SS have higher rates of depression than patients with other organ involvement, suggesting an organic cause for depression. History, physical examination, and laboratory testing can diagnose exacerbations of medical illness and provide evidence of focal CNS involvement. Clinical experience suggests that, in the absence of an SLE flare, mood disorders may be treated with antidepressants. Most affective disorders that arise in the context of a systemic SLE flare may be treated with a combination of immunosuppressive treatment (for example, corticosteroids, cyclophosphamide) and adjunctive psychotropic medications.

Additionally, disturbances in mood and cognition may be provoked by certain medications (for example, corticosteroids). Psychiatric disorders are associated with prednisone doses of 40 mg/day and higher. Temporal relation between the mood symptoms and corticosteroid treatment and history of mood disorders with corticosteroid treatment help to clarify the diagnosis. Psychiatric symptoms appear early during corticosteroid treatment and resolve upon discontinuation.

The treatment of mood disorders includes use of psychopharmacological agents, talking therapies, electroconvulsive therapy (ECT), and neurosurgery. With recent advances in psychopharmacology, drug treatment of depression succeeds in up to 80% of cases.

Although no more efficacious than tricyclic antidepressants, selective serotonin reuptake inhibitors (SSRIs) are first line treatment for depression in rheumatological patients because of their safety record and tolerability. SSRIs lack the anticholinergic, orthostatic, and cardiac-
conduction-prolonging effects common with tricyclic antidepressants, but commonly cause gastrointestinal symptoms, headache, nervousness, and sexual dysfunction.

To treat depression you should aim for the therapeutic dose of the drug (for example, 20 mg of fluoxetine, paroxetine, or citalopram) as soon as the patient can tolerate it, continued for one year. The drugs used in this paradigm are only 3 of 20 equally efficacious available antidepressants; SSRI, tricyclic antidepressants, and monoamine oxidase inhibitors are equally effective in the treatment of major depression. Small doses (10–50 mg) of the tertiary amines (amitriptyline, imipramine, doxepin) may significantly affect mood. More sedating agents like mirtazapine, nefazodone, and nortriptyline may have a slight advantage. These drugs are used in this paradigm are only 3 of 20 equally effective available antidepressants; SSRI, tricyclic antidepressants, and monoamine oxidase inhibitors are equally effective in the treatment of major depression. Small doses (10–50 mg) of the tertiary amines (amitriptyline, imipramine, doxepin) may significantly relieve both insomnia and chronic pain suffered by patients with rheumatic diseases (table 1).

PSYCHOSTIMULANTS (FOR EXAMPLE, METHYLPHENIDATE (RITALIN), 5–20 MG, AND DEXTROAMPHETAMINE (DEXEDRINE), 2.5–10 MG) CAN BE DRAMATICALLY HELPFUL IN THE TREATMENT OF DEPRESSION IN ELDERLY, MEDICALLY ILL POPULATIONS, WITH RAPID IMPROVEMENT OF MOOD SYMPTOMS IN UP TO HALF OF PATIENTS. MOREOVER, THEY STIMULATE APPETITE AND WEIGHT GAIN IN ANOREXIC, CACHETIC PATIENTS AND PERMIT REDUCED DOSES OF OPiOID ANALGESICS WHILE REDUCING THEIR SEDATIVE EFFECTS AND LEAVING THE PATIENT MORE ALERT. ALTHOUGH STIMULANT USE MUST BE MONITORED IN PATIENTS WITH SEVERE HYPERTENSION AND VENTRICULAR IRRITABILITY, CLINICAL EXPERIENCE SHOWS THESE AGENTS TO BE REMARKABLY BENIGN.5

ECT IS PREFERRED FOR SEvere, LIFE THREATENING DEPRESSION, PSYCHOTIC DEPRESSION, AND WHEN DRUG TREATMENT IS JUDGED MORE DANGEROUS. EVEN PATIENTS WITH INCREASED INTRACRANIAL PRESSURE HAVE BEEN SAFELY TREATED.16

Two major psychotherapies have demonstrated effectiveness in the treatment of major depression in rheumatological patients: cognitive behavioural therapy (CBT), which deals with relations among affect, behaviour, and cognition, and interpersonal therapy (IPT), which deals with interpersonal relationships. In CBT, the patient learns to identify how the negative view of self, world, and future escalates to unwarranted generalisations (for example, “she snubbed me” to “nobody loves me”) and worsens mood. Patients learn to challenge and change this sequence. IPT is an equally commonsense process that deals with the current problem (for example, functional disability) and its impact on the patient’s relationships both at home and at work and how these relationships affect to mood.

Education about the symptoms and signs of depression is a major component of any psychotherapy for a depressed patient. During a mood episode, the patient should not make major life changes. Spouses and other family members benefit from periodic education and reassurance that they are not responsible for their loved one’s illness. Treatment continues until recovery is complete. As depression tends to recur, it is important for patients and physicians to recognise recurrent symptoms so that treatment can be resumed immediately.

PATIENTS WITH FIBROMYALGIA REQUIRE A COMBINED TREATMENT APPROACH. IMPROVEMENT WILL COME FASTER IF THEY CAN ACCEPT THAT RESTORATION OF FUNCTION (FOR EXAMPLE, TO MOVE, WALK, WORK, PLAY), NOT PAIN RELIEF, IS THE PRIMARY GOAL OF TREATMENT. IMPROVEMENT OF SLEEP, REGULAR EXERCISE, AND TREATMENT OF DEPRESSION (WHEN PRESENT) ARE INDISPENSABLE. NO ANTIDEPRESSANT HAS DEMONSTRATED SUPERIORITY AND REASSURANCE THAT THEY ARE NOT RESPONSIBLE FOR THEIR LOVED ONE’S ILLNESS.

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Table 1 Commonly used antidepressants

<table>
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<tr>
<th>T1/2 (h)</th>
<th>Sedative potency</th>
<th>Anticholinergic potency</th>
<th>Orthostatic hypotension</th>
<th>Cardiac arrhythmia potential</th>
<th>Initial dose (mg/day)</th>
<th>Dose range (mg/day)</th>
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</thead>
</table>
| **SSRIs**
| Fluoxetine | 87 | + | + | 4/− | +/− | 20 | 20–80 |
| Sertraline | 26 | + | + | 4/− | +/− | 50 | 50–200 |
| Paroxetine | 21 | +/++ | ++ | 4/− | +/− | 10 | 10–60 |
| Fluvoxamine | 19 | + | + | 4 | + | 50 | 50–300 |
| Citalopram | 35 | + | + | + | +/− | 10 | 10–60 |
| **Tricyclics**
| Doxepin | 17 | +++ | ++ | ++ | + | 50 | 75–400 |
| Amitriptyline | 21 | +++ | +++ | +++ | + | 50 | 75–300 |
| Imipramine | 18 | +++ | ++ | ++ | + | 50 | 75–300 |
| Trimipramine | 13 | +++ | ++ | +++ | + | 50 | 75–300 |
| Clomipramine | 23 | ++ | +++ | +++ | + | 50 | 75–300 |
| **Tertiary amines**
| Amoxapine | 8 | ++ | ++ | − | + | 200 | 75–300 |
| Propranolol | 78 | + | +++ | + | + | 15 | 15–60 |
| Propripranolol | 30 | ++ | ++ | + | + | 25 | 40–150 |
| Desipramine | 21 | + | ++ | +++ | + | 50 | 75–300 |
| **Secondary amines**
| Maprotiline | 43 | +++ | ++ | − | + | 75 | 75–225 |
| Trandol | 3.5 | +++ | +/− | + | + | 30 | 50–600 |
| Bupropion | 15 | + | + | 4/− | − | 75 | 75–300 |
| Venlafaxine | 3.6 | + | + | + | + | 75 | 75–375 |
| Nefazodone | 3 | ++ | + | + | + | 150 | 150–600 |
| Mirtazapine | 30 | ++ | + | + | + | 15 | 15–45 |
| **MAOIs**
| Phenelzine | + | + | +++ | − | 30 | 30–90 |
| Tranylcypromine | + | + | +++ | + | 10 | 10–60 |

1, t1/2 = elimination half life; = none; = lowest; = low; = moderate; = high. Edwin Cassem (Adapted from Richelson E, Mayo Clin Proc 1994;69:1069–81).
is resistant and the depression does not respond to two or more adequate trials of antidepressants, referral to a psychiatrist would be appropriate.

Although rheumatic diseases and psychiatric disorders are commonly comorbid, depression may not be recognised. Timely recognition and determined treatment can reduce the distress, despair, and dysfunction that cripple these patients' lives.

MENEKSE ALPAY
EDWIN H CASSEM
Massachusetts General Hospital, Warren 604, Fruit Street, Boston, MA 02114, USA

Correspondence to: Dr Alpay