Depressed patients referred to psychiatrists have nearly always failed to respond to first-line treatment with antidepressant medication. Subsequent care by the psychiatric team will involve a comprehensive care package; however, for most patients the adjustment of antidepressant medication will also play an important role.

The use of medication in treatment-resistant depression has benefited from the availability of an increasing number of antidepressant drugs. However, the evidence base for treating resistant depression is slight. Furthermore, it is difficult to produce treatment algorithms that can be broadly applicable; each patient must be treated as an individual and a collaborative approach pursued.

What is treatment-resistant depression?

- Treatment-resistant depression is not ‘all or none’ but is best conceptualised as a series of stages within which patients have failed to respond to an increasing number of therapeutic approaches.
- Many of these stages consist of pharmacological interventions. This module has focused on pharmacological treatment, but other approaches are also important. The use of supportive psychotherapy can help a despairing patient persist in treatment and eventually improve.
- Current practice identifies different stages of treatment resistance as:
  - failure to respond to a single antidepressant treatment
  - failure to respond to two antidepressant treatments
  - failure to respond to three antidepressant treatments, at least one of which is from a different pharmacological class (e.g. two SSRIs and mirtazapine).

Switching antidepressants

- When switching antidepressants, the first switch can be within the same class, but subsequent switches should be to a different pharmacological class.
- It is important that treatment-resistant patients receive an antidepressant trial with potentially more effective agents than standard SSRIs.
- Venlafaxine is more effective than SSRIs, but not amitriptyline. While SSRIs are regarded as having relatively flat dose-response curves, both amitriptyline and venlafaxine are more effective at higher doses in some patients.
- MAOIs may be suitable for any form of major depression that has failed to respond to three or four classes of antidepressant drugs, particularly atypical depression (overeating, oversleeping, rejection sensitivity) and bipolar depression.

Augmentation

- Augmentation:
  - can be useful in more treatment-resistant patients
  - can be helpful when there is a partial response to antidepressant treatment
  - is quicker to implement than other treatments
  - can involve the addition of an antidepressant (e.g. mirtazapine to SSRI)
  - can involve the addition of an agent that is not regarded as an antidepressant in its own right (e.g. lithium).

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• Lithium is a reasonably well-established augmentation therapy.

• Antipsychotic drugs have an established role in the treatment of depressive psychosis, and it is important to detect psychotic symptoms in patients with resistant depression.

• The addition of atypical antipsychotic medication to SSRI/SNRI treatment may be helpful in non-psychotic treatment-resistant depression.

Other therapies and depression in bipolar illness

• In treatment-resistant patients, other kinds of therapy may also be effective.

• Electroconvulsive therapy (ECT) can be effective in more treatment-resistant patients, particularly in patients with depressive psychosis and/or psychomotor retardation.

• Cognitive-behaviour therapy (CBT) can also play a useful role in the treatment of resistant depression at any stage if the patient wishes to try it and the treatment is available.

• It is important to assess depressed patients for the presence of bipolar traits. Depression in bipolar illness can be difficult to treat with antidepressant medication as a number of problems can arise.

Further reading
