

Depression

causes, presentation and treatment

Depression is common, serious and treatable

The current National Depression Initiative aims to increase public recognition of this important condition, leading to earlier presentation and treatment.

Depression affects not only the individual, but also those around them. It decreases motivation, tolerance and concentration. This impairs parenting and relationships. It also affects productivity and safety at work. It causes the loss of over a million working days a year in New Zealand and decreased productivity on twice that number of days. The recent New Zealand mental health epidemiology study found nearly 6% of adults had experienced major depression in the last year, and 16% during their lifetime.¹

Multifactorial causes

The final pathway for depression is presumably disturbed neurotransmission, but how a variety of stressors cause this is unclear. Some people are more vulnerable to depression due to genetic factors, past adversity or previous episodes of depression. Resilience built through overcoming challenges and good social support can reduce this risk. Whether a particular stressor triggers depression may depend on the meaning of the particular event for the individual; whether it occurs alone or along with other pressures; and the person's overall social context. Losses, such as a relationship ending, bereavement, unemployment, financial or legal problems, or loss of health, are common triggers. Physical illness, such as hypothyroidism or Parkinson's Disease, can lead to depression directly, while any chronic or life-threatening illness can cause considerable emotional strain. Some medications can cause depression, such as steroids, oral contraceptives and some beta-blockers.

Presentations vary

The core features of depression are EITHER low mood, **or** loss of all interest and pleasure in usually pleasurable activities, persistently and pervasively over at least two weeks **and** which significantly impairs a person's social or occupational functioning. Associated with this are other symptoms, summarised in the box below.

- significant weight loss or gain (when not dieting) or marked change in appetite
- insomnia or hypersomnia nearly every day
- psychomotor agitation or retardation nearly every day
- fatigue or loss of energy nearly every day
- feelings of worthlessness or excessive or inappropriate guilt nearly every day
- diminished ability to think or concentrate, or indecisiveness, nearly every day
- recurrent thoughts of death (not just fear of dying), recurrent suicidal ideation without a specific plan, or a suicide attempt or a specific plan for committing suicide

(Criteria summarised from DSM-IV)²

So, while one often thinks of a person suffering depression as being slowed up, sleeping poorly and losing weight, they can be gaining weight, sleeping excessively and agitated. Adolescents can present as irritable rather than overtly depressed.

Depression may also occur as part of other psychiatric disorders. The clinical presentation is very similar, but the distinction has important treatment implications.

Treatment

This must start with a thorough clinical assessment. This should establish the type of depression; the person's strengths and supports; contributing causes to their depression; and ways the person and those close to them can work to change or adjust to these. An assessment of risk of suicide, or risk to others through neglect of usual caregiving roles, is essential.

Information that depression is a clinical condition, not a moral weakness or personal failure, is important, as is the expectation of effective treatment. Clinical support to review current stressors and their resolution is essential. For mild to moderate depression, structured brief psychotherapies such as cognitive behaviour therapy are as effective as antidepressant medication. They may offer protection against future episodes by providing effective self-treatment. However its availability is limited, particularly in the public sector.

There is an increasing range of antidepressant medications. The major groups are:

- Selective Serotonin Reuptake Inhibitors (SSRIs)
- Tricyclic antidepressants (TCAs)
- Selective Serotonin and Noradrenaline Reuptake Inhibitors (SNRIs, e.g venlafaxine)
- Reversible Inhibitors of Monoamine Oxidase A (RIMAs, e.g moclobemide)
- Irreversible Monoamine Oxidase Inhibitors (older and now rarely used)

Most of these groups have recently been reviewed by bpac¹² in the best practice journal.³ Newer agents are generally more tolerable than older ones, although there is a rare risk of agitation and increased suicidality with SSRIs.

Mechanism of action

Current theories of drug action emphasise interactions with subpopulations of serotonin and noradrenaline receptors. However, it is important to recognise that there are many other neurotransmitters affecting regulation of mood. Antidepressants also affect the levels of brain derived neurotrophic factor, which is a locally active agent that influences the production of new axonal connections and may have a significant part to play in the recovery from depression.⁴ Investigations into these other mechanisms controlling mood can be expected to lead to more effective treatments in the future.

Choosing an antidepressant

There is no compelling evidence that one drug or drug group is more effective or better tolerated than another so choice of antidepressant is based on individual patient factors and includes:

- **Previous response** If a patient has responded well to an antidepressant before, that drug should be considered as first choice.
- **Adverse effects** Drugs which have previously caused troublesome or unmanageable adverse effects should be avoided. The drug's adverse effect profile and its potential for aggravating any concurrent conditions should be considered. For example, avoiding TCAs in cardiac conduction abnormalities.
- **Assessment of potential for drug interactions** For example, citalopram has a much lower potential for interactions than fluoxetine or venlafaxine.
- **Individual tolerance to adverse effects** For some people the anticholinergic effects of TCAs will be unacceptable but others will not tolerate the stimulatory effects sometimes associated with SSRIs.
- **Co-morbid psychiatric or medical conditions may influence drug choice**
- **Starting and continuing treatment** If a person's drug taking is erratic and unreliable, fluoxetine may be the preferred SSRI as it has a long half-life and is less likely to cause discontinuation effects.
- **Suicide risk** The potential for fatal overdose is much higher with TCAs than with SSRIs. Suicidal thinking has been linked to SSRIs but this can also occur with TCAs and any antidepressant drug treatment.

Optimising response

Optimising the response to antidepressant treatment involves initial drug choice as outlined above, use of an adequate dose for sufficient duration, management of adverse effects, review of diagnosis, management of patient expectations and the use of concurrent non-drug treatment. It is very important to explain to patients the possibility of non-drug options to augment antidepressants and the expectations of antidepressant therapy. A person's expectations and beliefs about their condition and treatments can influence compliance.

Appropriate dose and duration

Antidepressants should usually be started at the recommended initial dose and the response reviewed after 4–6 weeks. With TCAs, gradual titration every 3–7 days is generally recommended to assess tolerance of dose related side effects. A smaller initial dose should be considered in some situations, e.g. if there is associated panic disorder or anxiety or if the person has previously found drug treatment intolerable.

If response to an antidepressant is poor, partial or not sustained after 4–6 weeks, compliance and review of diagnosis needs to be checked before a change is considered. Some patients may also respond to an increase in dose according to the manufacturer's recommendations. Temporary dose reduction to manage adverse effects may be warranted. For example, if an SSRI causes initial mild restlessness (not associated with severe anxiety or suicidal ideation), reducing the dose or short term use of a benzodiazepine may be effective instead of switching to an alternative drug.

Changing drug therapy

If there is a partial response, or an initial response that has become attenuated, a further increase in dose may be effective. If there is no response at all to the usual maximum dose then a response may be obtained by changing to another drug.

There are no hard and fast rules to guide which drug to switch to. Similar factors that governed the initial drug choice may be relevant and there may be some logic in trying a drug from a different class. However, a response or better tolerability is often seen by changing to another drug from the same class, (e.g. switching from fluoxetine to citalopram). This may be explained by subtle differences in pharmacology or differences in drug metabolism and genetic polymorphism. When switching drugs, consideration needs to be given to washout periods, cross tapering and the management of discontinuation syndrome.

Getting well, staying well

Treatment of major depression aims to achieve complete remission of symptoms. This may require a trial of more than one agent. Response rates of about two-thirds can be expected with any of these agents in primary care, with an effective treatment possible for some 90% of depressed people. Relapse rates are high — up to 50% in the first year after recovery — so continued treatment at the effective treatment dose is important. After recurrent depression, there is evidence to support continued treatment for up to three years. Drug interactions are important. While CYP2D6 is a common mechanism of metabolism, some agents, such as citalopram, are metabolised by CYP3A4, with a different pattern of interactions. Strategies to cope with side-effects, or to change medication, help people continue with their treatment.

Interventions in the pharmacy

In the pharmacy, if there is concern about someone's safety when collecting their antidepressant, it can be helpful to ask the person how they are and if they feel safe. If they express concern, one can ask if they can get help for this. Are they planning to discuss this with the doctor or mental health team, or do they have friends, family or whānau to call on? All mental health services have crisis teams who can be contacted in emergencies, whether or not an individual is currently using their services.

References

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