CHAPTER 8

SADNESS AND DEPRESSION

[Please note: Two depression scales are available, after the references. Readers may choose to print the text only, without these additional pages.]

Introduction

In the current era, there is a tendency to "medicalize" the human condition (Summerfield, 2006). By this is meant, certain aspects of "normal" human behaviour and experience get "re-badged" as medical conditions. An example: what was formerly described as promiscuous or self indulgent sexual behaviour is being "diagnosed" in pop-psychology as "sexual addiction". Chapter 32 deals in detail with "medicalization" in detail.

It is profoundly important that we understand that sadness (depressed mood) is a part of the human experience – when people a sad for good reason we should give them support, but we must not call them "sick" until they have sufficient symptoms to justify the diagnosis.

From the beginning of this chapter, we need to be aware that very clever people continue to make the point that we should not consider every person who is experiencing an unpleasant experience, a "patient". Sociologists Horwitz & Wakefield (2007) wrote the important book, "The Loss of Sadness: How psychiatry transformed normal sorrow into depressive disorder". This title carries a powerful message. More recently, distinguished psychiatrist Allen Frances (2013) wrote the book "Saving Normal" – in which he demonstrates that many normal reactions are being called illness/sickness.

Does it matter what is "normal" and "abnormal"? At times when medicine is generally considered to be limited to the abnormal, yes, it does. An example: Medicare covers the cost of only certain cosmetic surgery procedures - it will cover the cost of repairing a face damaged by an accident, but not the passage of time (a face-lift for loss of skin elasticity).

But the contrary view, that the distinction between normal and abnormal is unimportant, can be argued. The modern practitioner is expected to provide comfort and assistance to those in need, and the prevention of disease is regarded as a greater good than its treatment. Example: the management of obesity and mild elevation of the blood pressure, neither of which are diseases, are legitimate activities for medical practitioners.

We will look briefly at the experiences of sadness, grief and demoralization, but will, of course, spend the majority of our energy on the pathological conditions which have sadness as a prominent feature.

As we know, the current diagnostic systems (DSM-5, ICD-10) are descriptive. McHugh (2005) states the time has come to move to an etiological perspective. His proposed etiological approach involves 4 clusters: 1) "brain disease", in which there is disruption of neural underpinnings, 2) "vulnerability because of psychological make-up", 3) the adoption of behaviour "that has become a relatively fixed and warped way of life", and 4) "conditions provoked by events that thwart or threaten".

With respect to "depression", Cluster 1 would include severe depressive disorder (such as psychotic, for example), Cluster 2 would incorporate the low mood associated with some personality types, Cluster 3 would incorporate the depression which is secondary to, or associated with, conditions including alcoholism, pathological gambling and anorexia nervosa, and Cluster 4 would incorporate the low mood of grief, situational anxiety and posttraumatic disorder. Such a system of classification would assist in indicating the most appropriate professional response.

Sadness

We have all experienced sadness, the undesired emotion which accompanies undesired events, such as loss of a valued object or individual, or failure to achieve a desired goal. While healthy people report days when they are "a bit down" for no apparent reason, in healthy people, deeper and longer-lasting sadness occurs only as a reaction to events.

In the mood disorders, the mood may shift excessively in response to a minor event, or in the complete absence of a triggering/stimulating event, and once established the excessive/pathological mood remains.

Grief/Bereavement

Grief is the term applied to the unpleasant experience of having lost a close person (usually a friend or family member, but this can be associated with the loss of a public figure). Also, this experience can result from the loss of inanimate objects, such as a collection of valuable art works gathered over a lifetime.

Grief is emotional pain, accompanied by a longing for the return of the lost object, and a feeling of emptiness and incompleteness. In Western cultures there may be crying, insomnia and loss of appetite. There may be a sense of guilt at being alive in the absence of the lost person, and auditory and visual hallucinations of the lost person are not unusual in the early period (and are not evidence of psychosis).

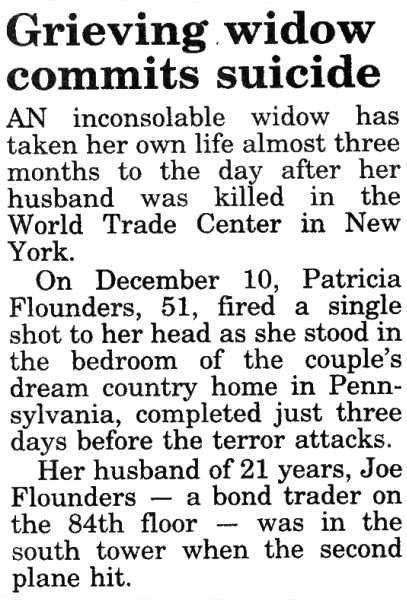
Culture influences both the expression and experience of grief. Some cultures have clear rules for the behaviour and dress of the bereaved, and even the precise length of time for the grieving/mourning process. The details may vary depending on the nature of the relationship (universally, spouses grieve longer than siblings). There are advantages to having culturally approved grieving protocols. The bereaved individual, who is distressed and finds making decisions difficult, has a clear script/ritual to follow. Adhering to the ritual ensures that no one is offended during this time of emotional arousal. Also, once all steps/obligations have been fulfilled there is an

official end point to the grieving, and the bereaved person is allowed/expected to return to their usual life. A structured grieving process (uncommon in Western cultures) reduces the likelihood of "delayed" or "pathological" grief.

DSM-5 advises that grief may lead into major depressive disorder, the clinician needs to be alert to this possibility and offer treatment for unnecessary/additional suffering.

The grief reaction is considered to have become "pathological" when it persists longer than usual or has unusual features (Nakamura, 1999). There is concern when the grief is not abating some months after the death. It is generally believed (in the West) the grieving process, in the case of a spouse, takes 6 to 12 months. Grief and pathological grief are yet to be clearly differentiated. For example, what does "recovery" mean following the loss of a spouse of 50 years?

The bereaved individual who has not eaten or slept and is inconsolable one week after the event is probably suffering excessively. While a sense of guilt at having survived is not uncommon, any delusions of guilt should be regarded at pathological.



Grieving widow commits suicide

AN inconsolable widow has taken her own life almost three months to the day after her husband was killed in the World Trade Center in New York.

On December 10, Patricia Flounders, 51, fired a single shot to her head as she stood in the bedroom of the couple's dream country home in Pennsylvania, completed just three days before the terror attacks.

Her husband of 21 years, Joe Flounders — a bond trader on the 84th floor — was in the south tower when the second plane hit.

Illustration. The loss of a spouse may lead to suicide – is this pathological grief?

Demoralization

Demoralization has been described as being distinct from major mental disorder (Clarke & Kissane, 2002).

An English dictionary definition of demoralize: "to deprive a person of spirit, courage or discipline; to reduce to a state of weakness or disorder".

Demoralization has been most commonly discussed as a consequence of unremitting, unavoidable stress. It has most often been described in the context of chronic physical or psychiatric disorders, but is reported in a range of adverse situations (Gutkovich et al, 1999).

Animal studies yield the notion of "learned helplessness" (Seligman, 1975). If an animal is subjected to inescapable stress (an electrified cage floor), it eventually stops trying to escape and "gives up" (quivering and inactive). It has been suggested that 'learned helplessness' may be a model for battered wife syndrome. Learned helplessness is a better model for demoralization than depression.

Frank (1974) observed that demoralization "results from persistent failure to cope with internally or externally induced stresses that the person and those close to him expect him to handle". The features include feelings of "impotence, isolation, and despair", damaged self-esteem, and a sense of "alienation" or "meaninglessness of life".

Slavney (1999) stated that in demoralization, "the mood is sad, apprehensive or irritable; thinking is pessimistic and sometimes suicidal; behaviour can be passive, demanding, or uncooperative; and sleep and appetite are often disturbed".

Clark et al (2000) studied hospitalized medically ill patients and found the concepts of demoralization, grief and anhedonia (the inability to experience pleasure, a central feature of depressive disorders) to be separate dimensions.

Patfield (2000) argued that suicidal behaviour is related to a sense of helplessness and alienation rather than a direct consequence of depressed mood. Butterworth et al (2006) more recently confirmed an association between demoralization and suicidal behaviour.

Gutkovich et al (1999) studied émigrés in USA. They were able to categorize a large proportion of people as manifesting, 1) depression and no demoralization, 2) demoralization and no depression, and 3) with both.

Commonly used psychological instruments do not allow the differentiation of demoralization from depression (Loxton et al, 2006).

Current evidence suggests that demoralization is a separate entity from depression. Of course, the adversity which triggers demoralization may also trigger depression, and demoralization may be a risk factor for depression. The appeal of the concept of demoralization is that as the condition arises out of adversity and the perception of the individual that he/she is powerless to influence his/her situation, effective management programs should be possible, using established psychotherapy principles (Clarke & Kissane, 2002; de Figueiredo & Gostoli, 2013).

Depression

In this section, those psychiatric disorders will be outlined in which the mood is changed to sad or low. It is most important to be aware that in these disorders, mood change is not the only symptom; others include vegetative symptoms such as sleep and appetite change. Thus, these disorders are diagnosed using batches or patterns of symptoms (not simply low mood alone).

The main disorders include major depressive disorder (also termed unipolar depression – such patients do not experience excessive mood elevation), persistent depressive disorder (which is similar to, but the symptoms are not as severe major depressive disorder, and bipolar depression (this is the depressive phase or a disorder which also has pathological mood elevation). DSM-5 has included "Premenstrual Dysphoric Disorder" within the depression group of disorders. This inclusion will not be universally supported (Weisz and Knaapen, 2009).

Major depressive episode

A major depressive episode is a batch of symptoms, and is similar for major depressive disorder and bipolar depression (which can only be diagnosed when a manic episode has occurred).

Criteria for major depressive episode:
At least one of the following for at least 2 weeks:

- persistent depressed mood
- loss of interest and pleasure.

At least four of the following for at least 2 weeks:

- significant weight loss or gain
- insomnia or increased sleep
- agitation (worrying and physical restlessness) or retardation (slowed thinking and moving)
- fatigue or loss of energy
- feelings of worthlessness or inappropriate guilt
- diminished ability to concentrate or indecisiveness
- thoughts of death or suicide.

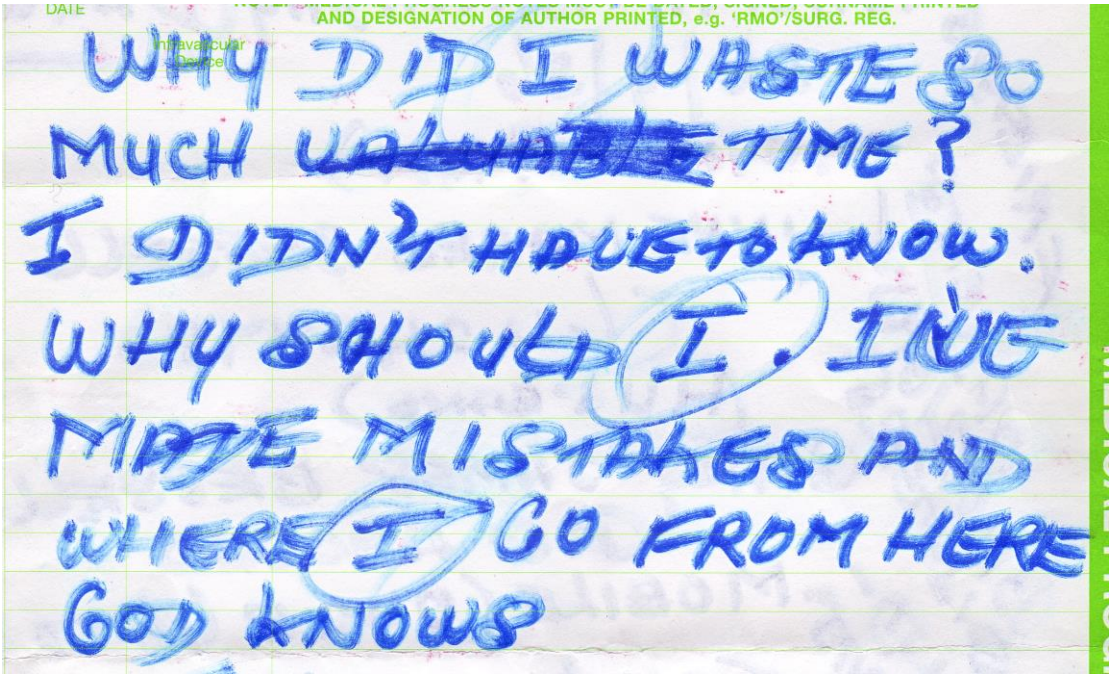


Illustration. This was written by a 65-year-old female with severe depression. Depressed people do not write a lot of notes, they usually lack energy and initiative, but this person was agitated and restless. This is a rare example of someone expressing unjustified guilt feelings (as a result of depression). She is self critical, stating that she has wasted time. She circles the letter "I" on two occasions, to emphasise that she identifies herself as being at fault. She states that she has made mistakes, and she is uncertain/pessimistic about the future.

Major depressive disorder [MDD]

MDD is diagnosed when there has been one or more major depressive episodes and no history of mania or hypomania.

This serious disorder causes great suffering. The prevalence in western societies is 5.4 to 8.9 % (Narrow et al, 2002) [at a gut level, this seems improbably high to the current author]. A recent study found that close to half the population can expect one or more episodes of depression during their lifetime (Andrews et al, 2005). The prevalence of depressive disorder is twice as common in females. The average age of onset is in the mid-20s.

80% of people who suffer a major depressive episode will have recurrent episodes.

1/3 of people with MDD do not achieve remission despite multiple treatment trials, and a further 1/3 suffer relapses despite continued adherence to treatment (Rush et al, 2006).

Cognitive deficits sufficient to cause occupational impairment have been identified in people with MDD (including those in remission) (Woo et al, 2016).

It has long been believed that 15% of people with either major depressive disorder or bipolar disorder die by suicide, however, recent work gives the much lower figure of 3.4% (Blair-West & Mellsop, 2001)

Aetiology - Biological

Aetiology of major depressive disorder is unknown.

A vast number of possible roles for biological mechanisms have been suggested, including:

- neurotransmitters: serotonin, norepinephrine, dopamine, glutamate acetylcholine and GABA somatostatin, corticotrophin and substance P.
- receptors (Pytka et al, 2016).
- trophic factors (Sharma et al, 2016).
- ceremides (lipid components of neurons; Garcia-Garcia et al, 2011).
- vitamin D deficiency (Anglin et al, 2013).
- "gut-brain axis" (Foster et al, 2013).
- epigenetic factors (Mahgoub & Monteggia, 2013).
- peripheral inflammation (Byrne et al, 2016).
- glial synaptic dysfunction (Rial et al, 2016).

Multiple theories link various biological mechanisms:

- Gut bacteria (microbiota) impacting on the the vagus nerve and immune system.
- inflammatory mediators (IL-1, IL-6, TNF-alpha, CRP), the endocrine system and neurotransmitters (Becking et al, 2015; Muneeer, 2015; Bhattacharya et al, 2016).
- Heritability in the range 31-42% (Ebmeier, et al, 2006). A multitude of genes with small effect are likely to be involved, which interact with environmental factors.

Aetiology – Social/Psychological

Child abuse and neglect is universally accepted as a powerful etiological factor in some cases of depressive disorders, and in those cases in which it is a feature, the prognosis is much less favourable (Nemeroff, 2016).

Other risk factors include neurotic personality traits, low self-esteem, early onset anxiety, a history of conduct disorder, substance misuse, adversity, interpersonal difficulties, low education, lifetime trauma, low social support, divorce and stressful life events (Kendler, et al, 2006).

Post-mortem studies

In a post-mortem study of anterior cingulate cortex (ACC) in mood disorder, although layer thickness was unchanged, there was decreased density of glial cells across all layers. The density of pyramidal neurons and the shapes of neurons differed in some layers (ittens and Harrison, 2011).

Neuroimaging

Some neuroimaging reports on "depression" do not make a clear distinction between MDD and bipolar depression. Such studies are mentioned under this heading. Studies dealing specifically with bipolar depression are listed under the later heading: **Bipolar depression.**

White matter hyperintensities (or white matter lesions) are discrete regions which appear brighter on T2-weighted MRI scans (reflecting a localized change in water content in that tissue). While hyperintensities are associated with increasing vascular disease and age, they have a clear association with major depressive disorder and bipolar depression (Videbech, 1997). A longitudinal study demonstrated that white matter changes pre-date, and may be causally related to depressive symptoms (Teodorczuk et al, 2007).

MDD diffusion tensor imaging studies (DTI) have shown wide spread white matter abnormalities in first-episode medication naïve patients (Wu et al, 2011).

A DTI study ventral tegmentum (a primary component of the subcortical reward/aversion circuitry) in MDD demonstrated microstructural abnormalities (Blood et al, 2011). A recent DTI study demonstrated altered orbitofrontal cortex

connection with other brain structures in treatment naïve people with depression (Long et al, 2014).

MRI studies in MDD have demonstrated reduction in hippocampal size (Campbell et al 2004; Saylam et al, 2006).

Anterior cingulate cortex (ACC) has received much imaging attention. An ACC based neural network (including various other areas of prefrontal cortex, amygdala, hippocampus, striatum and thalamus) may have a central role in mood disorders (Drevets and Savitz, 2008; Sexton et al, 2013). ACC grey matter reduction, blood flow and metabolism alterations and glial cell reduction have been reported.

Repeated stress can lead to dendritic atrophy and reduction in glial cells (in rodents). This may result from increased glutamate stimulation and glucocorticoid release. The ACC contains cortisol receptors (which turn off cortisol), and damage to the ACC could result in a positive feedback loop with ever increasing cortisol release, and emotional dysregulation.

In a meta-analysis of magnetic resonance spectroscopy (MRS) studies, the ACC of people with MDD, has been found to contain low concentrations of glutamate and glutamine during depressive episodes (Luykx et al, 2011).

Abnormalities have been demonstrated in the ACC and the hippocampus (temporal lobe). A recent study of the 'uncinate fasciculius' (see illustration in Chapter 5) which connects these two structures demonstrates structural abnormalities and increased functional connectivity in major depression (Kawaasteniet et al, 2013).

In summary, neuroimaging studies in mood disorder are yielding rich scientific information, but this has not yet been translated into clinical applications. There is widespread loss of white and grey matter and alterations in chemical composition and metabolism. ACC has received particular attention, and loss of glia in this structure has been suggested, abnormalities of the uncinated fasciculus (linking ACC and hippocampus) may be significant.

Cognition

In acute major depression, 63% of people have cognitive difficulties (compared to 3.3% of controls, $p<0.001$; Afridi et al, 2011). Attention/concentration is the domain most commonly affected, followed by memory disturbance.

Neurocognitive deficits may be present during remission, are independent of mood status, and may cause occupational impairment (Neu et al, 2001; Jaeger et al, 2006; Woo et al, 2016)

'Mentalizing' is the subject of Chapter 33 and is an alternative to the term 'Theory of Mind' – the ability of the individual to understand the minds of others. A recent study of females with MDD (compared to controls; Fischer-Kern et al, 2013) found a significantly lower 'mentalizing', and deficits were related to illness duration and number of hospitalizations.

Treatment

The etiological approach of McHugh (2005) assists in treatment.

Cognitive behaviour therapy (CBT) is a form of psychotherapy which may be effective in mild/moderate depression (Cuijpers et al, 2010). The theoretical basis of CBT is that depressive symptoms arise from dysfunctional beliefs and thought processes which are the results of past experience and learning. The aim of CBT is to identify these negative thoughts and replace them with informed and logical thinking habits.

According to some authorities (Karyotaki et al, 2016) psychotherapy is as effective as medication in the acute phase and superior to medication in the long term. According to these authors combining psychotherapy and medication provides no benefits. [At a gut level, this seems improbable to the current author.]

Medication is recommended in the treatment of moderate and severe depression. However, as mentioned above, the efficacy of current antidepressants is disappointing (Rush et al, 2006; Bschor and Kilarski 2016).

Chapter 16 (Antidepressant drugs) also provides additional information.

Selective serotonin reuptake inhibitors (SSRIs), which increase the concentration of serotonin in the synaptic clefts (fluoxetine, paroxetine, fluvoxamine, citalopram and sertraline), are the most widely used. Dual action agents increase availability of both serotonin and norepinephrine (venlafaxine and mirtazapine, among others) are perhaps more potent than the SSRIs.

Agomelatine has some SSRI activity but is also novel in being an agonist of melatonin receptors. Evidence suggests an antidepressant action (Taylor et al, 2014) – but, its usefulness has been challenged (Urade et al, 2015; Yatham et al, 2016).

Older medications include the tricyclic antidepressants (TCAs) and monoamine oxidase inhibitors (MAOIs) are less commonly used at the current time, because they have more side-effects and present a greater risk in overdose. However, they are effective and continue to be used by some specialist practitioners.

In recent years, the NMDAR antagonist, ketamine, has been administered intravenously for rapid remission of MDD, which has not been responsive to other treatments (Duman and Aghajanian, 2012; Wohleb et al, 2016).

Other non-drug, physical treatments of unremitting depression include electroconvulsive therapy (ECT) and transcranial magnetic stimulation (TMS) – see Chapters 28 & 29.

Bipolar depression

Much of what appears under the heading of MDD also applies in bipolar depression.

The elevated phases of bipolar disorder is discussed in greater depth in Chapter 9.

Over recent years, authorities have argued that it is important to distinguish MDD from bipolar depression, because the treatment of bipolar depression may precipitate an episode of mania (Post, 2006).

Accordingly, there have been attempts to identify clinical features which may differentiate bipolar depression from major depressive disorder. To the present time there has been no success.

Aetiology – biological
Aetiology – social/psychological

What appears above which respect to aetiology of MDD applies in most cases with equal force to bipolar depression.

Cognition

Neurocognitive deficits have been quantified (Czobor et al, 2007).

Histology

Post-mortem study of the hippocampus in bipolar disorder has shown specific alteration of interneurons, including a reduction in somal volume and numbers (Konradi et al, 2011).

Neuroimaging

A meta-analysis of brain structure in people with bipolar disorder (CT and MRI; Kempton et al, 2008) incorporating the results of almost 100 studies (3509 patients) found, 1) bipolar disorder was associated with increase lateral ventricle enlargement ($P=8X10^{-7}$), and 2) increased rates of deep white matter hyperintensities ($P=2X10^{-5}$). In comparison with controls, patients had a lateral ventricular enlargement of 17%, and a deep white matter hyperintensities rate of 250%. These structural findings can be accepted as being beyond doubt.

Grey matter defects are widespread (Li et al, 2011b). Progressive hippocampal, parahippocampal and cerebellar grey matter loss has been associated with deterioration in cognitive function and illness course (Moorhead et al, 2007).

Corpus callosum (CC) MRI studies in bipolar disorder have been reviewed (Arnone et al, 2008), finding decreases in CC areas, suggesting reduced integration of the hemispheres.

As mentioned above, there is interest in being able to distinguish between MDD and bipolar depression, but this has proven difficult/impossible using clinical symptoms. Attempts are now being made to make this distinction using imaging. A recent study examined interhemispheric connectivity in three groups, 1) MDD, 2) bipolar depression and 3) healthy controls. The pathological groups could be distinguished from the healthy controls, but no could not be distinguished from each other (Wang et

al, 2015). However, in a recent functional (f)MRI study, MDD and bipolar depression patients "could be clearly distinguished" (from each other) "by changes in large-scale networks" (Goya-Maldonado et al, 2016).

Treatment

Mood stabilizing drugs (with which we attempt to clamp the mood in the euthymic position, neither too high nor too low) are central to the treatment of bipolar disorder. They include lithium carbonate, the anticonvulsants carbamazepine, sodium valproate, and lamotrigine, and some atypical antipsychotics, including olanzapine, quetiapine and perhaps others.

Antidepressants appear able to trigger manic swings in people with bipolar disorder. Thus, there is reluctance to treat bipolar depression with an antidepressant without first commencing a mood stabilizer.

When treating bipolar depression, some experts (R M Post, personal communication) first add a second mood stabilizer. If there is little response, an antidepressant is then tried. In patients known to have been catapulted into mania by antidepressants in the past, other choices include making the patient as comfortable as possible and waiting for natural resolution of the episode, or moving to TMS or ECT.

The NMDAR antagonist, ketamine, has been administered intravenously for rapid remission of bipolar depression, with good effect (Duman and Aghajanian, 2012; Wohleb et al, 2016).

Persistent depressive disorder

There are no blood or other objective tests for the mental disorders. This makes psychiatry difficult (and interesting). Objective tests would be particularly useful in the area between normal sadness and major depressive disorder.

Persistent depressive disorder is diagnosed when some symptoms of MDD (but not sufficient for a diagnosis of MDD) have persisted for 2 years. This condition may represent a mild form of MDD or incomplete remission from MDD. The prognosis of major depressive disorder is less than ideal; 30-50% of patients will still have substantial residual symptoms after adequate first-line treatment, and a poor outcome occurs in at least 25% of patients at 12-year follow-up (Surtees & Barkley, 1994).

Personality is discussed in Chapter 10. Personality is the constellation of behaviour/reactions which make us different from each other. Just as individuals differ in their capacity for honesty and generosity, so too, do they differ in their capacity for cheerfulness, optimism and energy. Those who by nature/make-up are at the low end of the cheerfulness scale may satisfy the diagnosis of persistent depressive disorder.

Treatment

Somewhat surprisingly, given that psychotherapy is said to be indicated in "mild to moderate depression", psychotherapy as the sole treatment of persistent depressive disorder yields relatively poor results (Markowitz, 1994). The SSRIs may be useful. Most are treated with a combination of an SSRI and cognitive-behaviour orientated therapy (to assist with self-esteem and adjustment).

Hamilton depression rating scale

Many different scales are used in the assessment of depression. The Hamilton Depression Rating Scale (HDRS, or HAM-D (D for depression); Hamilton also created an anxiety scale) has been widely used for more than 5 decades (Hamilton, 1960). It is rated by trained professionals.

The HDRS is not used to make a diagnosis, but to rate severity. Serial ratings over time reflect change (hopefully, improvement). The diagnosis must be made before the HDRS is applied. Because it relies on many vegetative symptoms, the HDRS is not applicable when there is a concurrent severe medical disorder.

The original HDRS consisted of 21 items, however, a shorter 17 item version is commonly used.

Even though the HDRS is not used for diagnosis, many researchers have come to equate a score of 8 with remission. To ensure subjects have at least moderate depression, many studies require an entry score 18.

A COPY OF THE HDRS FOLLOWS THE REFERENCES

Montgomery Asberg depression rating scale

The Montgomery Asberg Depression Rating Scale (MADRS; Montgomery & Asberg 1979) is a second important depression scale. It followed almost two decades after the HDRS, but has been widely used over the last quarter of a century.

In contrast to the HDRS, the MADRS focuses less strongly on the somatic symptoms of depression, and more strongly on items such as concentration difficulties, tension, lassitude, pessimistic and suicidal thoughts.

The initial hope was that being less focused on somatic symptoms, the MADRS would be more sensitive to change than the HDRS. This has not been substantiated.

A COPY OF THE HDRS AND MADRS FOLLOW THE REFERENCES

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HAMILTON DEPRESSION RATING SCALE (HAM-D)

Hamilton M.
A rating scale for depression

Journal of Neurology, Neurosurgery and Psychiatry 1960: 23:56-62

Patient Information													
Patient		**Date**	**Day**		**Mth**		**Year**		**Time**	**Hour**		**Min**	
Personal notes													

TICK APPROPRIATE BOX FOR EACH ITEM

1. Depressed mood This item covers both the verbal and the non-verbal communication of sadness, depression, despondency, helplessness and hopelessness.	
0 - Neutral mood.	☐
1 – When it is doubtful whether the patient is more despondent or san than usual, e.g. the patient vaguely indicates to be more depressed than usual.	☐
2 – When the patient more clearly is concerned with unpleasant experiences, although he still is without helplessness or hopelessness.	☐
3 – The patient shows clear non-verbal signs of depression and/or is at times overpowered by helplessness or hopelessness.	☐
4 – The patient's remarks on despondence and helplessness or the non-verbal ones dominate the interview in which the patient cannot be distracted.	☐

2. Self-depreciation and guilt feelings This item covers the lowered self-esteem with guilt feelings.	
0 – No self-depreciation or guilt feelings.	☐
1 – Doubtful whether guilt feelings are present, because the patient is only concerned with the fact that he, during the actual illness, has been a burden to the family or colleagues due to reduced work capacity.	☐
2 – Self-depreciation or guilt feelings are more clearly present because the patient is concerned with incidents in the past prior to the actual episode, e.g. the patient reproaches himself small omissions or failures, not to have done his duty or to have harmed others.	☐
3 – The patient suffers from more severe guilt feelings. He may express that he feels that the actual suffering is some sort of a punishment. Score 3 as long as the patient intellectually can see that his view is unfounded.	☐
4 – The guilt feelings are firmly maintained and resist any counterargument, so that they have become paranoid ideas.	☐

3. Suicidal impulses	
0 – No suicidal impulses.	☐
1 – The patient feels that life is not worth while, but he expresses no wish to die.	☐
2 – The patient wishes to die, but has no plans of taking his own life.	☐
3 – It is probably that the patient contemplates to commit suicide.	☐
4 – If during the days prior to the interview the patient has tried to commit suicide or if the patient in the ward is under special observation due to suicidal risk.	☐

4 - 6: Note: Administration of drugs – sedative or others – shall be disregarded.

4. Initial insomnia	
0 – Absent.	☐
1 – When the patient 1 (1-2) out of the last 3 nights has had to lie in bed for more than 30 minutes before falling asleep.	☐
2 – When the patient all 3 nights has been in bed for more than 30 minutes before falling asleep.	☐

5. Middle insomnia The patient wakes up one or more times between midnight and 5 a.m. (If for voiding purposes followed by immediate sleep rate O). .	
0 – Absent.	☐
1 – Once or twice during the last 3 nights.	☐
2 – At least once every night.	☐

6. Delayed insomnia = Premature awakening The patient wakes up before planned by himself or his surroundings.	
0 – Absent.	☐
1 – Less than 1 hour (and may fall asleep again).	☐
2 – Constantly – or more than 1 hour too early.	☐

7. Work and interests This item includes both work carried out and motivation. Note, however, that the assessment of tiredness and fatigue in their physical manifestations is included in item 13 (general somatic symptoms) and in item 23 (tiredness and pain). **A. At first rating of the patient**	
0 – Normal work activity.	☐
1 – When the patient expresses insufficiency due to lack of motivation, and/or trouble in carrying out the usual work load which the patient, however, manages to do with reduction.	☐
2 – More pronounced insufficiency due to lack of motivation and/or trouble in carrying out the usual work. Here the patient has reduced work capacity, cannot keep normal speed, copes with less on the job or in the home; the patient may stay home some days or may try to leave early.	☐
3 – When the patient has been sick-listed, or if the patient has been hospitalised (as day activities).	☐
4 – When the patient is fully hospitalised and generally unoccupied without participation in the ward activities.	☐
B. At weekly ratings	
0 – Normal work activity, a) The patient has resumed work at his normal activity level: b) When the patient will have no trouble to resume normal work.	☐
1a) – The patient is working, but at reduced activity level, either due to lack of motivation or due to difficulties in the accomplishment of his normal work: **b)** The patient is not working and it is still doubtful that he can resume his normal work without difficulties.	☐
2a) – The patient is working, but at a clearly reduced level, either due to episodes of non-attendance or due to reduced work time: **b)** The patient is still hospitalised or sickened, participates more than 3-4 hours per day in ward (or home) activities, but is only capable to resume normal work at a reduced level. If hospitalised the patient is able to change from full stay to day-patients status.	☐
3 – When the patient has been sick-listed, or if the patient has been hospitalised (as day activities).	☐
4 – When the patient is fully hospitalised and generally unoccupied without participation in the ward activities.	☐

8. Retardation (general)	
0 – Normal verbal activity, normal motor activity with adequate facial expression.	☐
1 – Conversational speed doubtfully or slightly reduced and facial expression doubtfully or slightly stiffened (retarded).	☐
2 – Conversational speed clearly reduced with intermissions, reduced gestures and slow pace .	☐
3 – The interview is clearly prolonged due to long latencies and brief answers' all movements very slow.	☐
4 – The interview cannot be completed, retardation approaches (and includes) stupor.	☐

9. Agitation	
0 – Normal motor activity with adequate facial expression.	☐
1 – Doubtful or slight agitation, e.g. tendency to changing position in chair or at times scratching his head .	☐
2 – Fidgeting, wringing hands, changing position in chair again and again. Restless in ward, with some pacing.	☐
3 – Patient cannot stay in chair during interview and/or much pacing in ward.	☐
4 – Interview has to be conducted "on the run". Almost continuous pacing. Pulling off clothes, tearing his hair.	☐

10. Anxiety (psychic) This item includes tenseness, irritability, worry, insecurity, fear and apprehension approaching overpowering dread. It may often be difficult to distinguish between the patient's experience of anxiety ("Psychic" or "central" anxiety phenomena) and the physiological ("peripheral") anxiety manifestations which can be observed, e.g. hand tremor and sweating. Most important is the patient's report on worry, insecurity, uncertainty, experiences of dreadfulness, i.e. the psychic ("central") anxiety.	
0 – The patient is neither more nor less insecure or irritable than usual.	☐
1 – It is doubtful whether the patient is more insecure or irritable than usual.	☐
2 – The patient expresses more clearly to be in a state of anxiety, apprehension or irritability which he may find difficult to control. It is thus without influence on the patient's daily life, because the worrying is still about minor matters.	☐
3 – The anxiety or insecurity is at times more difficult to control, because the worrying is about major injuries or harms which might occur in the future, e.g. the anxiety may be experienced as panic, i.e. overpowering dread. Has occasionally interfered with the patient's daily life.	☐
4 – The feeling of dreadfulness is present so often that it markedly interferes with the patient's daily life.	☐

11 Anxiety (somatic) This item includes physiological concomitants of anxiety: All feeling states should be rated under item 10 and not here.	
0 – When the patient is neither more nor less prone than usual to experience somatic concomitants of anxiety feeling states.	☐
1 – When the patient occasionally experiences slight manifestations like abdominal symptoms, sweating or trembling. However, the description is vague and doubtful.	☐
2 – When the patient from time to time experiences abdominal symptoms, sweating, trembling, etc. Symptoms and signs are clearly described, but are not marked or incapacitating, i.e. still without influence on the patient's daily life.	☐
3 – Physiological concomitants of anxious feeling states are marked and sometimes very worrying. Interferes occasionally with the patient's daily life.	☐
4 – The feeling of dreadfulness is present so often that it markedly interferes with the patient's daily life.	☐

12. Gastro-Intestinal Symptoms may stem from the entire gastro-intestinal tract. Dry mouth, loss of appetite and constipation are more common than abdominal cramps and pains. Must be distinguished from gastro-intestinal anxiety symptoms ("butterflies in the stomach" or loose bowel movements) and also from nihilistic ideas (no bowel movements for weeks or months; the intestines have withered away) which should be rated under 15 (Hypochondriasis).	
0 – No gastro-intestinal complaints (or symptoms unchanged from before onset of depression).	☐
1 – Eats without encouragement by staff and food intake is about normal, but without relish (all dishes taste alike and cigarettes are without flavour). Sometimes constipated.	☐
2 – Food intake reduced, patient has to be urged to eat. As a rule clearly constipated. Laxatives are often tried, but are of little help.	☐

13. General Somatic Central are feelings of fatigue and exhaustion, loss of energy. But also diffuse muscular achings and pains in neck, back or limbs, e.g. muscular headache.	
0 – The patient is neither more nor less tired or troubled by bodily discomfort than usual.	☐
1 – Doubtful or very vague feelings of muscular fatigue or other somatic discomfort.	☐
2 – Clearly or constantly tired and exhausted and/or troubled by bodily discomforts e.g. muscular headache.	☐

14. Sexual interests This subject is often difficult to approach, especially with elderly patients. In males try to ask questions concerning sexual preoccupation and drive, in females responsiveness (both to engage in sexual activity and to obtain satisfaction in intercourse).	
0 – Insufficient information or uncertainty. No loss of interest.	☐
1 – Probable loss of interest related to depression.	☐
2 – Certain pronounced loss of interest related to depression.	☐

15. Hypochondriasis Preoccupation with bodily symptoms or functions (in the absence of somatic disease).	
0 – The patient pays no more interest than usual to the slight bodily sensations of every day life.	☐
1 – Slightly or doubtfully more occupied than usual with bodily symptoms and functions.	☐
2 – Quite worried about his physical health. The patient expresses thoughts of organic disease with a tendency to "somatise" the clinical presentation.	☐
3 – The patient is convinced to suffer from a physical illness which can explain all his symptoms (brain tumour, abdominal cancer etc), but the patient can for a brief while be reassured that this is not the case.	☐
4 – The preoccupation with bodily dysfunction has clearly reached paranoid dimensions. The hypochondriacal delusions often have a nihilistic quality or guilt associations: to be rotting inside; insects eating the tissues; bowels blocked and withered away, other patients are being infected by the patient's bad odour or his syphilis. Counter-argumentation is without effect.	☐

16. Loss of insight This item has, of course, only meaning if the observer is convinced that the patient at the interview still is in a depressive state.	
0 – The patients agreed to having depressive symptoms or a "nervous" illness.	☐
1 – The patient still agrees to being depressed but feels this to be secondary to non-illness related conditions like malnutrition, climate, overwork.	☐
2 – Denies being ill at all. Delusional patients are by definition without insight. Enquiries should therefore be directed to the patient's attitude to his symptoms of Guild (item 2) or Hypochondriasis (item 15), but other delusional symptoms should also be considered.	☐

17. Weight loss Try to get objective information. If such is not available be conservative in estimation. **A. At first interview this item covers the whole actual period of illness.**	
0 –No weight loss.	☐
1 – 1-2.5 kg weight loss.	☐
2 – Weight loss of 3 kg or more.	☐
B. Weekly interviews	
0 –No weight loss.	☐
1 – 1-2.5 kg weight loss.	☐
2 – 1 kg or more per week.	☐

MONTGOMERY-ASBERG DEPRESSION RATING SCALE (MADRAS)

Montgomery S, Asberg M
British Journal of Psychiatry
1979; 134:382-389

Patient Information													
Patient		**Date**	**Day**		**Mth**		**Year**		**Time**	**Hour**		**Min**	
Personal notes													

TICK APPROPRIATE BOX FOR EACH ITEM

1. Apparent sadness Representing despondency, gloom and despair (more than just ordinary transient low spirits), reflected in speech, facial expression and posture. Rate by depth and inability to brighten up.	
0 = No sadness.	☐
2 = Looks dispirited but does brighten up without difficulty.	☐
4 = Appears sad and unhappy most of the time.	☐
6 = Looks miserable all the time, Extremely despondent.	☐

2. Reported sadness Representing reports of depressed mood, regardless of whether it is reflected in appearance or not. Includes low spirits, despondency or the feely of being beyond help and without hope.	
0 = Occasional sadness in keeping with the circumstances.	☐
2 = Sad or low but brightens up without difficulty.	☐
4 = Pervasive feelings of sadness or gloominess. The mood is still influenced by external circumstances.	☐
6 = Continuous or unvar4ying sadness, misery or despondency.	☐

3. Inner tension Representing feelings of ill-defined discomfort, edginess, inner turmoil, mental tension mounting to either panic, dread or anguish. Rate according to intensity, frequency, duration and the extent of reassurance called for.	
0 = Placid. Only feeling inner tension.	☐
2 = Occasional feelings of edginess and ill-defined discomfort.	☐
4 = Continuous feelings of inner tension or intermittent panic which the patient can only master with some difficulty.	☐
6 = Unrelenting dread or anguish. Overwhelming panic.	☐

4. Reduced sleep Representing the experience of reduced duration or depth of sleep compared to the subject's own normal pattern when well.	
0 = Sleeps as normal.	☐
2 = Slight difficulty dropping off to sleep or slightly reduced, light or fitful sleep.	☐
4 = Moderate stiffness and resistance.	☐
6 = Sleep reduced or broken by at least 2 hours.	

5. Reduced appetite Representing the feeling of a loss of appetite compared with when-well. Rate by loss of desire for food or the need to force oneself to eat. .	
0 = Normal or increased appetite.	☐
2 = Slightly reduced appetite.	☐
4 = No appetite. Food is tasteless.	☐
6 = Needs persuasion to eat at all.	

6. Concentration difficulties Representing difficulties in collecting one's thoughts mounting to an incapacitating lack of concentration. Rate according to intensity, frequency and degree of incapacity produced.	
0 = No difficulties in concentrating.	☐
2 = Occasional difficulties in collecting one's thoughts.	☐
4 = Difficulties in concentrating and sustaining thought which reduced ability to read or hold a conversation.	☐
6 = Unable to read or converse without great difficulty.	

7. Lassitude Representing difficulty in getting started or slowness I initiating and performing everyday activities.	
0 = Hardly any difficulty in getting started. No sluggishness.	☐
2 =Difficulties in starting activities.	☐
4 = Difficulties in starting simple routine activities which are carried out with effort.	☐
6 = Complete lassitude. Unable to do anything without help.	☐

8. Inability to feel Representing the subjective experience of reduced interest in the surroundings, or activities that normally give pleasure. The ability to react with adequate emotion to circumstance or people is reduced.	
0 = Normal interest in the surroundings and in other people.	☐
2 = Reduced ability to enjoy usual interests.	☐
4 = Loss of interest in the surroundings. Loss of feelings for friends and acquaintances. .	☐
6 = The experience of being emotionally paralysed, inability to feel anger, grief or pleasure and a complete or even painful failure to feel for close relatives and friends.	☐

9. Pessimistic thoughts Representing thoughts of guilt, inferiority, self-reproach, sinfulness, remorse and ruin.	
0 = No pessimistic thoughts.	☐
2 = Fluctuating ideas of failure, self reproach or self-depreciation.	☐
4 = Persistent self-accusations or definite but still rational ideas of guilt or sin. Increasingly pessimistic about the future. .	☐
6 = Delusions of ruin, remorse or irredeemable sin. Self-accusations which are absurd and unshakable.	☐

10. Suicidal thoughts Representing the feeling that life is not worth living, that a natural death would be welcome, suicidal thoughts and preparation for suicide. Suicide attempts should not in themselves influence the rating.	
0 = Enjoys life or takes it as it comes.	☐
2 = Weary of life. Only fleeting suicidal thoughts.	☐
4 = Probably better off dead. Suicidal thought are common and suicide is considered as a possible solution, but without specific plans or intentions. .	☐
6 = Explicit plans for suicide when there is an opportunity. Active preparations for suicide.	☐