Chapter 4 Mood disorders

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### Depressive disorder

#### Epidemiology

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<th></th>
<th>Incidence</th>
<th>Lifetime prevalence</th>
<th>Point prevalence</th>
<th>Age of onset</th>
<th>Gender ratio</th>
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<tr>
<td>International</td>
<td>14.0 per 1000 persons</td>
<td>Overall: 10-20%; 1 in 4 women and 1 in 10 men have depressive disorder in their lifetime.</td>
<td>2-5%</td>
<td>25-45 years</td>
<td>F:M = 2:1</td>
</tr>
<tr>
<td>Singapore</td>
<td>As above</td>
<td>As above</td>
<td>5.6%</td>
<td>As above</td>
<td>As above</td>
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#### Aetiology

**Genetics:**
1) Family studies show that a person has 40-70% chance to develop depressive episode if a first degree relative suffer from depressive episode.
2) Twin studies show that the concordance rate for monozygotic twins is 40 – 50% and for dizygotic twins is 20%.
3) Adoption studies show that the risk to develop depressive disorder of adoptees with family history of depressive disorder is twice as high as in adoptees without family history of depressive disorder.

**Organic causes:**
1) Physical illnesses include Cushing’s syndrome, Addison’s disease, Parkinson’s disease, stroke, epilepsy, coronary arterial disease and hypothyroidism
2) Medications: Corticosteroids, oral contraceptive pills, beta-blockers, clonidine, metoclopramide, theophylline and nifedipine

**Psychosocial factors:**
(a) Adversity in childhood
   - Maternal loss and disruption of bonding.
   - Poor parental care and over-protection among parents.
   - Childhood physical and sexual abuse.

(b) Adversity in adulthood
   - Women: Absence of a confiding relationship, having more than 3 children under the age of 14 and unemployment (Brown and Harris’ social origins of depression, 1978).
   - Men: Unemployment, divorce (e.g. unable to pay for maintenance fees and loss of custody).
Recent life events
- Loss of a child.
- Death of a spouse.
- Divorce.
- Martial separation.
- Imprisonment.
- Recent death of a close family member.
- Unemployment.

**Neurobiology of depressive disorder:**
1. Monoamine theory states that depressed patients have decreased levels of noradrenaline, serotonin and dopamine. Evidence include the finding that the 5-HIAA levels are reduced in the CSF of depressed patients who committed suicide. 5-HIAA is a metabolite of serotonin. The tricyclic antidepressants increase noradrenaline levels. The selective serotonin reuptake inhibitors increase the serotonin levels. The antidepressant bupropion may increase dopamine levels.
2. Other neurotransmitters include raised acetylcholine levels (associated with depressive symptoms such as anergia, lethargy, psychomotor retardation) and decreased levels of gamma-aminobutyric acid (GABA).
3. Neuroendocrinology: Elevated CRF, ACTH and cortisol in blood and CSF in depressed patients. Non-suppression in dexamethasone suppression test (DST) is greatest in people with severe depression and reversed with antidepressant treatment. Non-suppression of DST is a result of increased hypothalamic CRF release. Depression reduces the level of inhibitory hormone, somatostatin and increases the level of growth hormone. Decreased levels of thyroid hormone ($T_4$) are associated with depressive symptoms.
4. Neuroimaging: Ventricular enlargement, sulcal widening and reduction in size in the frontal lobe, cerebellum, basal ganglia, hippocampus and amygdala.

**ICD-10 and DSM-IV-TR criteria**

Summary of ICD-10 F32.0 Mild, F32.1 Moderate, F32.2 Severe (Bold + Italic) criteria diagnostic criteria of depressive disorder in four axes (RATA). The RATA axis: Reality (hallucinations and delusions); Appearance and behaviour; Thought and speech; Affect and interest.

<table>
<thead>
<tr>
<th>General appearance</th>
<th>Thoughts</th>
<th>Affect</th>
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<tbody>
<tr>
<td>- Not specified by ICD – 10 or DSM IV TR</td>
<td>- Recurrent thoughts of death or suicide</td>
<td>- Depressed mood most of the day, almost every day for 2 weeks (CORE criteria)</td>
</tr>
<tr>
<td>- Neglect of dressing &amp; grooming</td>
<td>- Diminished ability to think and concentrate</td>
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<tr>
<td>- Turning downwards of the corners of the mouth</td>
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<tr>
<td>- Vertical furrowing of the centre of brow &amp; gaze is downwards</td>
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**Hallucination**

**Condemnatory auditory hallucinations**

**Reality axis**

**Interest**

1. Loss of interest or pleasure in activities that are normally pleasurable (CORE criteria)
2. Decreased energy or increased fatigability (CORE criteria)

**Speech** Depressive stupor

**Delusion**

1. Guilt
2. Hypochondriasis
3. Nihilistic
4. Self referential
5. Persecutory

**Behaviour**

1. Loss of confidence or self esteem
2. Unreasonable feelings of self reproach or excessive guilty
3. Psychomotor agitation or retardation
4. Sleep disturbance
5. Change in appetite
6. Somatic syndrome
For ICD – 10, mild depressive disorder requires 2 out of 3 core criteria + 2 remaining criteria; moderate depressive disorder requires 2 out of 3 core criteria + 4 remaining criteria; severe depressive disorder requires 3 out of 3 core criteria + 6 remaining criteria + psychotic features.

Other criteria for DSM-IV TR Major Depressive Episode include weight loss; significant distress in social and occupational functioning; not due to substance, medical condition, or bereavement.

**OSCE grid: Assess depression.**

You are the resident working in the AED. A 30 – year - old teacher is referred by polyclinic for management of depression. He cannot cope with the workload and he also has interpersonal problems with the school principal.

Task: To a history to establish the diagnosis of depressive disorder.

Please note that forgetting to have a brief assessment of suicidal risk in a depressed patient may result in a failure.

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<tr>
<td></td>
<td>‘During the past month, how often have you been bothered by feeling down or depressed?’</td>
<td>‘Have your energy levels been recently?’</td>
<td>‘Can you tell me more about your interests and hobbies before the current depressive episode?’</td>
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<tr>
<td></td>
<td>‘Can you rate your current mood from a scale of 1 to 10? 1 means very depressed and 10 means very happy.’</td>
<td>‘Do you feel tired most of the time?’</td>
<td>‘During the past month, how often have you been bothered by having little interest or pleasure in doing things?’</td>
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<td></td>
<td>‘Which part of the day is the worst?’ (Elicit diurnal variation of mood)</td>
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<td></td>
<td>‘How has your sleep been lately?’</td>
<td>‘Has your appetite changed recently? If yes, do you tend to eat less or more?’</td>
<td>I hope you would not mind if I ask you some sensitive questions such as sexual problems as depression may affect sexual function. Is it OK with you?</td>
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<td>‘Can you fall asleep? If not, how long does it take?’</td>
<td>‘Has your weight changed recently? If so, have you lost weight or gained weight. If yes, how many kilograms were involved?’</td>
<td>‘Have there been any changes in your sexual function recently? If yes, can you tell me more about the nature of sexual dysfunction?’</td>
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<td></td>
<td>‘How many times do you wake up in the middle of the night? (exclude urination)’</td>
<td></td>
<td>‘When did the sexual dysfunction start? (Does it coincide with the onset of depression?)’</td>
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<td></td>
<td>‘What time do you wake up in the morning? (look for early morning wakening). If you wake up, can you fall asleep again?’</td>
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<td></td>
<td>‘What has your concentration been like recently? Can you concentrate when you teach?’</td>
<td>‘How do you see yourself?’</td>
<td>‘Can you tell me more about your negative thoughts?’</td>
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<td></td>
<td></td>
<td>‘Do you see yourself a failure?’</td>
<td>Look for selective abstraction,</td>
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<tr>
<td>D. Assess risk, psychotic features, insight.</td>
<td>E. Explore causes and background.</td>
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<tr>
<td><strong>D1. Assess suicide risk.</strong></td>
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<tr>
<td>‘Have you felt that life is not worth living?’</td>
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<tr>
<td>‘Would you do anything to harm yourself or hurt yourself?’</td>
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<tr>
<td>‘Have you done anything of that sort? Have you made any plans? Have you told anybody about it?’</td>
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<td><strong>D2. Assess psychotic features.</strong></td>
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<tr>
<td>‘When people are under stress, they complain of hearing voices or believing that other people are doing something to harm him. Do you have such experiences?’</td>
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<td><strong>D3. Assess insight</strong></td>
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<tr>
<td>‘What is your view of the current problem? Do you think that you may suffer from a depressive illness?’</td>
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<tr>
<td><strong>E1. Explore family history of depression.</strong></td>
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<tr>
<td>‘Do you have any biologically related relative suffer from depression?’</td>
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<tr>
<td>‘Do you have any biologically related relative attempt or commit suicide in the past?’</td>
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<tr>
<td><strong>E2. Explore past psychiatric history and relevant medical illnesses.</strong></td>
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<tr>
<td>‘Did you seek help from a psychiatrist or GP in the past for your low mood?’</td>
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<tr>
<td>‘Did you receive any treatment from a psychiatrist? If yes, can you tell me more about the medication and side effects?’</td>
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<tr>
<td>‘How anxious do you feel in yourself?’ (explore comorbidity)</td>
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<tr>
<td>‘Do you drink alcohol on a daily basis to cope with stress or help you to sleep?’</td>
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<tr>
<td>‘Do you suffer from any chronic medical illness?’</td>
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<tr>
<td><strong>E3. Assess support system.</strong></td>
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<tr>
<td>‘Can you tell me the person who is providing emotional support to you at this moment?’</td>
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<td>‘Is there a person in the school whom you can talk to?’</td>
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<tr>
<td>‘What is your career plan at this moment?’</td>
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<tr>
<td>‘Have you sought help from Ministry of Education?’</td>
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**Compare and contrast ICD-10 and DSM-IV criteria for depressive disorder**

**Summary other types of depressive disorder in ICD-10 & DSM-IV-TR**

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<th>Severity of depressive illness</th>
<th>ICD – 10</th>
<th>DSM IV</th>
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<td>Mild depressive episode.</td>
<td></td>
<td>Major depressive disorder single or recurrent episode.</td>
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<tr>
<td>Moderate depressive episode with or without somatic symptoms</td>
<td></td>
<td>Mild, moderate, severe without psychotic or with psychotic features.</td>
</tr>
<tr>
<td>Severe depressive episode with or without psychotic symptoms.</td>
<td></td>
<td>With catatonic features.</td>
</tr>
<tr>
<td>Recurrent</td>
<td>At least one episode of mild, moderate &amp; severe</td>
<td>Separate mood episodes with an interval of at least 2 years.</td>
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<tr>
<td>depressive disorder</td>
<td>depression lasting 2 weeks and separate from the current episode by at least 2 months. Recurrent episodes of depressive reaction, psychogenic, reactive and seasonal depressive disorder. No history of manic or hypomaniac episode. It often associates with short period of anxiety and risk for deliberate self harm.</td>
<td>consecutive months. Recurrent with catatonic, melancholic, atypical features or postpartum onset.</td>
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<tr>
<td>Cyclothymia</td>
<td>A persistent instability (2 years) of mood involving numerous periods of depression and mild elation but not severe for diagnosis of bipolar disorder or depressive disorder. Some people have cyclothymic personality.</td>
<td>At least 2 years for adult, 1 year for children &amp; adolescents. Similar to ICD – 10 criteria</td>
</tr>
<tr>
<td>Dysthymia</td>
<td>There must be a period of at least 2 years of constant or constantly recurring depressed mood while normal mood rarely lasts longer than a few weeks.</td>
<td>At least 2 years for adult, 1 year for children &amp; adolescents. Poor appetite/overeating; insomnia/hypersomnia, fatigue, low self esteem, poor concentration, hopelessness. Early onset &lt; 21 years. Later onset &gt; 21 years.</td>
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<tr>
<td>Other mood disorders</td>
<td>Rapid alternation of hypomanic, manic or depressive symptoms within a few hours for at least 2 weeks. Recurrent brief depressive disorder which lasts less than 2 weeks.</td>
<td>Chronic depression: at least 2 years. Longitudinal course: with or without inter-episode recovery.</td>
</tr>
<tr>
<td>Melancholic depression</td>
<td>Not mentioned</td>
<td>1) Loss of pleasure in all activities. 2) Lack of reactivity to usually pleasurable stimuli. 3) Distinct quality of depressed mood. 4) Depression regularly worse in the morning. 5) Early morning awakening. 6) Marked psychomotor retardation. 7) Significant anorexia and weight loss. 8) Excessive or inappropriate guilt.</td>
</tr>
<tr>
<td>Atypical features</td>
<td>Not mentioned</td>
<td>Duration: 2 weeks 1) Mood brightens in response to actual or potentially positive events. 2) Hypersomnia. 3) Leaden paralysis in arms or legs. 4) Long standing pattern of interpersonal rejection sensitivity.</td>
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### Differential diagnosis

Differential diagnosis of depressive disorder includes:

1. Adjustment disorder, dysthymia, bipolar disorder, eating disorders, schizoaffective disorder, schizophrenia with predominance of negative symptoms.
2. Dementia, Parkinson’s disease, post-stroke depression and head injury in old people presenting with depression.
3. Addison’s disease, Cushing’s disease, hypothyroidism, parathyroid dysfunction, hypopituitarism and menopausal symptoms.
5. Syphilis and HIV encephalopathy.
6. Medication induced (e.g. beta-blockers, steroids, oral contraceptive pills)
7. Substance misuse (e.g. benzodiazepines, alcohol and opiates).

### Investigation

Routine laboratory tests should be ordered (e.g. FBC, ESR, B12/Folate, RFT, LFT, TFT, calcium panel and PTH). Sodium level is important in elderly who are prone to hyponatraemia as a result of SSRI treatment. Further investigations include urine drug screen, urine FEME and urine culture (for elderly), thyroid antibodies (for people with abnormal TFT), antinuclear antibody (suspected SLE) , syphilis Serology, HIV testing, CT/MRI.

### Questionnaire

**Beck Depression Inventory (BDI)**
The BDI is a 21-item self rate instrument to measure the presence and degree of depression in both adolescents (Reading age of approximately 10 years is required) and adults. It is self-rated and was designed to measure attitude and symptoms characteristic of depression. The BDI covers the 2 weeks prior to evaluation. It consists of 21 items, each categorised into various level of severity (with a range of score from 0 to 3). The total score is the sum of items. A total score <9 indicates no or minimal depression. A total score >30 indicates severe depression.

**Hamilton depression scale (HAM-D)**
The HAM-D scale is a clinician rated semi-structured scale. It is designed to measure the severity of depressive symptoms in patients with primary depressive illness. It has two versions: 17-item scale and 21-items scale. The 17-item version covers mood, suicide, guilt, sleep, appetite, energy, somatic complaints, sexual function and weight. The 21-item consists of addition 4 items on diurnal variation of mood, derealisation / depersonalisation, paranoid idea and obsession / compulsions. The HAM-D scale monitors changes in the severity of symptoms during treatment. The HAM-D scale is not diagnostic and its validity is affected if the person has concurrent physical illness. The total scores range from 0 (no depression), 0-10 (mild depression), 10-23 (moderate depression) and over 23 (severe depression).

**Montgomery-Asberg Depression Rating Scale (MADRS)**
The MADRS is a clinician-rated scale for patients with major depressive disorder. It measures the degree of severity of depressive symptoms and is a particularly sensitive measure of change in symptom severity during treatment. The 10-item checklist measures current mood state. In contrast to HAM-D, the MADRS is useful for people with concurrent physical illness as it puts less emphasis on somatic symptoms.

### Management

**[Mahendran and Yap (2005) and NICE guidelines (UK)]**

<table>
<thead>
<tr>
<th>Goal</th>
<th>The goal of treatment is to achieve symptomatic remission of all signs and symptoms of depression, restore occupational and psychosocial functioning.</th>
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</table>
| Initial treatment | • Counselling and supportive therapy alone may benefit those patients with mild depression.  
• If sleep is a problem, doctor should offer sleep hygiene advice.  
• If antidepressants are used as the first line of treatment. SSRI is the first line treatment. Tricyclic antidepressants (TCAs) must be avoided in suicidal patients because of their lethality in overdose. Doctors need to inform patient that the antidepressants will take 4 to 6 weeks to achieve its effect. Doctors should be familiar with side effects and be able to explain to patients about the side effects. Monotherapy with a single antidepressant is recommended.  
• In patients who are reluctant to start antidepressants, or patients with comorbid medical conditions who may be unable to tolerate the antidepressants, psychotherapy may be considered as a first-line treatment.  
• Hospitalisation may be required if the patient poses high suicide risk to self. |
| Acute phase of treatment | • The acute phase of treatment is accepted as lasting 12 weeks.  
• Efficacy of the treatment is gauged by amelioration of symptoms and the dose should be titrated according to clinical response.  
• Monitor all patients recently started on antidepressants closely for increased agitation and suicidal behaviour, especially young patients (younger than 25 years). |
- Some symptoms, such as sleep and appetite, may improve more quickly.
- If partial response or non-response, increase the dose or switch to another antidepressant. The first line is an alternative SSRI. The second line is an antidepressant from a different class.
- Doctors have to consider the half-life of the antidepressant before switching. A washout period is needed when switching from fluoxetine which has a long half-life and moclobemide (reversible MAOI) which requires a three-day washout period.
- If there is inadequate response to a single drug treatment, other agents such as another antidepressant (e.g. mirtazapine), mood stabiliser (e.g. lithium) or antipsychotics (e.g. olanzapine) can be added as augmentation therapy.
- Combination with psychotherapy such as cognitive behaviour therapy is recommended for patients with moderate depressive episode.

Stabilisation phase
- Antidepressants should be continued for at least six months after the acute phase.
- 3 to 4 months of psychological intervention is recommended for mild depressive episode.
- 4 to 6 months of psychological intervention is recommended for moderate and severe depressive episode.
- If a patient needs to stop antidepressants, stop gradually over a four-week period to avoid discontinuation symptoms. Common discontinuation symptoms include anxiety, giddiness, flu-like symptoms, low mood, nausea and insomnia. Antidepressants with shorter half-life such as paroxetine and venlafaxine need to discontinue over a longer period.

### Selective serotonin reuptake inhibitors (SSRIs)

<table>
<thead>
<tr>
<th>Indications</th>
<th>Contraindications</th>
<th>Mechanism of action</th>
<th>Side effects</th>
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<tbody>
<tr>
<td>Depressive disorder (first line treatment, less sedative than TCAs). Anxiety disorders</td>
<td>Mania</td>
<td>SSRIs selectively block reuptake of serotonin at presynaptic nerve terminals and increase synaptic serotonin concentrations</td>
<td>diarrhoea, constipation, weight loss.</td>
</tr>
<tr>
<td>Obsessive compulsive disorder Bulimia nervosa (fluoxetine) Premature ejaculation.</td>
<td></td>
<td></td>
<td>Agitation, tremor or insomnia. Sexual dysfunction</td>
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**Common SSRIs used in Singapore (2012 price in SGD)**

**Fluoxetine [Prozac]** (Dose range: 20 – 60mg/day; $0.46 for 10mg and $0.24 for 20mg)

**Special features** 1) Non linear elimination kinetics 2) Safe in overdose.

**Other indications**: 1) OCD (>60mg/day); 2) Panic disorder; 3) Bulimia Nervosa; 4) PTSD; 5) Premenstrual dysphoric disorder; 6) Premature ejaculation and 7) Childhood & adolescent depression.

**Pharmacokinetics**: 1) Fluoxetine inhibits the P450 3A3/4, 2C9, 2C19 & 2D6 and it also inhibits its own metabolism. 2) Due to non-linear pharmacokinetics, higher doses can result in disproportionately high plasma levels and of some side-effects (e.g. sedation) rather late in the course of treatment with this drug. Its metabolite norfluoxetine is much less potent. Long t½ = 72 hr.

**Pharmacodynamics**: The serotonin system exerts tonic inhibition on the central dopaminergic system. Thus, fluoxetine might diminish dopaminergic transmission leading to EPSE.

**Side effects**: 1) Anxiety, agitation 2) Delayed ejaculation/orgasmic impotence 3) Hypersomnolence (high doses) 4) Nausea 5) Dry mouth.

**Drug interaction**: 1) The washout period for fluoxetine before taking MAOI is 5 weeks. 2) Through inhibition of P450
2D6, fluoxetine may elevate the concentration of other drugs especially those with narrow therapeutic index such as flecainide, quinidine, carbamazepine and TCAs.

**Fluvoxamine [Faverin]** (Dose range: 50-300mg/day; $0.24 for 50mg)

**Special features:** 1) Highly selective SSRI 2) FDA approval for OCD 3) Lower volume of distribution, low protein binding and much shorter elimination half-life compared to SSRI.

**Other indications:** 1) Efficacious for social phobia 2) Panic Disorder 3) PTSD

**Pharmacokinetics:** 1) Well absorbed 2) $t_{1/2}$ =19 hours 3) metabolized to inactive metabolites. 4) lower volume of distribution and low protein binding 5) maximum plasma concentration is dose dependent. 6) Steady-state levels is 2 to 4-fold higher in children than in adolescents especially females. 7) Well tolerated in old people and in people with mild cardiovascular disease or epilepsy. 8) It offers potent inhibition of P450 1A2.

**Pharmacodynamics:** The specificity for 5HT re-uptake is greater for other SSRIs. Two neuro-adaptive changes: 1) specific serotonin receptor subtypes that change following presynaptic blockade 2) neurogenesis of hippocampal brain cells occurs and results in changes in behaviour.

**Side effect:** 1) Nausea – more common than other SSRIs; 2) Sexual side effects with fluvoxamine are similar in frequency to those with other SSRIs; 3) It minimal effects on psychomotor and cognitive function in humans.

**Sertraline [Zoloft]** (Dose range: 50-200mg/day; $1.92 for 25mg)

**Special features:** 1) For young women with mood disorders. 2) For mood and anxiety disorders.

**Other indications:** 1) Premenstrual dysphoric disorder 2) OCD 3) PTSD

**Pharmacokinetics:** 1) It inhibits P450 2C9, 2C19, 2D6, 3A4. 2) $t_{1/2}$ is 26 – 32 hours 3) More than 95% protein bound 4) Its metabolite, desmethylsertraline, is one-tenth as active as sertraline in blocking reuptake of serotonin.

**Pharmacodynamics:** The immediate effect of sertraline is to decrease neuronal firing rates. This is followed by normalization and an increase in firing rates, as autoreceptors are desensitized.

**Side effects:** 1)GI side effects 27%; 2) headache 26%; 3) Insomnia 22%; 4) Dry mouth 15% ; 5) Ejaculation failure 14%.

**Paroxetine CR [Seroxat CR]** (Dose range: 12.5-50mg/day; $2.23 for 12.5mg; $2.17 for 25mg)

**Special features:** 1) Most sedative and anticholinergic SSRI; 2) Risk of foetal exposure resulting in pulmonary hypertension

**Other indications:** 1) Mixed anxiety and depression; 2) Panic disorder; 3) social anxiety disorder; 4) generalised anxiety disorder 5) Post-traumatic stress disorder; 6) Premenstrual disorder

**Pharmacokinetics:** 1) Paroxetine is well absorbed from the GI tract. 2) it is a highly lipidophilic compound. 3) It has a high volume of distribution. 4) It is 95% bound to serum proteins. 4) It undergoes extensive first pass metabolism. 5) Paroxetine CR slows absorption and delay the release for 5 hours. 6) The Short $t_{1/2}$ of original paroxetine leads to discontinuation syndrome 7) It inhibits its own metabolism.

**Side effects:** 1) Anticholinergic side effects 2) Nausea 3) Sexual side effects emerge in a dose-dependent fashion 4) Closed angle glaucoma (acute). MOH guidelines state that first-trimester paroxetine use should be avoided, as it is associated with increased risk of serious congenital (particularly cardiac) defects.

**Drug interaction:** 1) Clinically significant interaction: MAOI, TCA, Type 1C antiarrhythmics, 2) Probably significant interaction: β-adrenergic antagonists, antiepileptic agents, cimetidine, typical antipsychotics, warfarin.

**Escitalopram [Lexapro]** (Dose range: 10-20mg/day; $1.5 for 10mg; $3.8 for 20 mg)

**Special features:** 1) Most selective SSRI 2) Relatively weak inhibition of liver P450 enzymes. 3) Escitalopram has fewer
side effects, more potent, shorter \( t_{1/2} \), less likely to inhibit P450 system, more selective than citalopram.

**Other indications:** 1) OCD 2) Panic Disorder 3) CVA 4) Anxiety with major depression 5) Emotional problems associated with dementia

**Pharmacokinetics:** 1) Escitalopram is well absorbed after oral administration with high bioavailability. 2) Peak plasma concentration is normally observed 2-4 hours following an oral dose. 3) It is subject to very little first-pass metabolism.

**Side effects:** Nausea and vomiting (20%), increased sweating (18%), dry mouth & headache (17%), anorgasmia and ejaculatory failure, but no significant effect on cardiac conduction and repolarisation.

**Trazodone** (Dose range: 150-300mg/day; this drug is not available at NUH)

**Special features:** trazodone is a mixed serotonin antagonist/agonist.

**Pharmacokinetics:** 1) Trazodone is well absorbed after oral administration, with peak blood levels occurring about 1 hour after dosing. 2) Elimination is biphasic, consisting of an initial phase \( t_{1/2} \) = 7 hours. 3) Its metabolites, mCPP, is a non-selective serotonin receptor agonist with anxiogenic properties.

**Pharmacodynamics:** Trazodone antagonises both \( \alpha_1 \) and \( \alpha_2 \) adrenoceptors but has very weak anticholinergic side-effects.

**Side effects:** 1) Priapism 2) Orthostatic hypotension 3) Increased libido 4) Sedation 5) Bone marrow suppression.

**Noradrenaline Specific Serotonin Antidepressant (NaSSa)**

**Mirtazapine** (Dose range: 15-45mg/day; $ 0.60/15mg)

**Special features:** 1) Mirtazapine blocks negative feedback of noradrenaline on presynaptic \( \alpha_2 \) receptors and activates noradrenaline system; 2) Mirtazapine stimulates serotonin neuron and increases noradrenaline activity; 3) Mirtazapine has no effects on seizure threshold or on cardiovascular system. 4) Suitable for patients who cannot tolerate SSRI induced sexual dysfunction.

**Other indications:** insomnia or poor appetite, dysthymia (40% reduction), PTSD (50% reduction) and chronic pain.

**Pharmacokinetics:** 1) The peak plasma level is obtained after approximately 2 hours. 2) Linear pharmacokinetics and a steady-state plasma level is obtained after 5 days. 3) The elimination \( t_{1/2} \) is 22 hours 4) Metabolised by P450 1A2, 2D6, and 3A4 4) 75% excreted by the kidney and 15% excreted by GI tract.

**Pharmacodynamics:** 1) Blockade of release-modulating \( \alpha_2 \)-adrenoceptors leads to enhanced noradrenaline release 2) the released noradrenaline stimulates serotonin neurons via the activation of \( \alpha_1 \) adrenoceptors which in turn results in an enhanced noradrenaline effect, together with the selective activation of 5-HT\(_{1A}\) receptors, may underlie the antidepressant activity; 3) 5HT\(_{1A}\) agonism: antidepressant and anxiolytic effects. 4) 5HT\(_{2A}\) antagonism: anxiolytic, sleep restoring and no sexual restoration 5) 5HT\(_{3c}\) antagonism: anxiolytic & weight gain 6) 5HT\(_{3}\) antagonism: no nausea, no gastrointestinal side effects. It also blocks histaminergic receptors and results in drowsiness.

**Side effects:** 1) drowsiness, 2) weight gain, 3) increased appetite, 4) dry mouth, 5) postural hypotension.

**Serotonin noradrenaline reuptake inhibitors (SNRIs)**

**Venlafaxine XR [Effexor XR]** (Dose range: 75mg – 375mg/day; $ 0.96/ 75mg tablet)

**Special features:** Low doses of venlafaxine blocks serotonin reuptake. Moderate doses of venlafaxine block noradrenaline reuptake. High dose of venlafaxine block noradrenaline, dopamine and serotonin reuptake. 2) Metabolised by P450 3A4 to inactive metabolites while P450 2D6 to active metabolites 3) More rapid onset action and enhanced efficacy in severe depression.

**Other indications:** generalised anxiety disorder.
Pharmacokinetics: 1) minimally protein bound (<30%) 2) renal elimination is the primary route of excretion 3) the original version (venlafaxine) has relatively short $t_{1/2} = 5-7$ hours; 4) prominent discontinuation syndrome (dizziness, dry mouth, insomnia, nausea, sweating, anorexia, diarrhoea, somnolence and sensory disturbance) and hence venlafaxine extended release (XR) is available.

Side effects: 1) nausea (35%); 2) sustained hypertension is dose related and 50% remitted spontaneously 4) dry mouth, constipation, 5) sexual dysfunction

Drug interaction: The toxic interaction with MAOIs, leading to a serotonin syndrome, is the most severe drug interaction involving venlafaxine.

Duloxetine [Cymbalta] (Dose range: 30-120mg/day; $3.8/30mg$ tablet)

Other indications: 1) Depression and chronic pain; 2) Fibromyalgia

Pharmacokinetics: Blood levels of duloxetine are most likely to be increased when it is co-administered with drugs that potently inhibit cytochrome P450 1A2.

Pharmacodynamics: Duloxetine exerts a more marked influence on noradrenaline reuptake than on serotonin reuptake.

Side effects 1) Nausea, dry mouth, dizziness, headache, somnolence, constipation and fatigue are common. 2) A small but significant increase in heart rate was observed 3) Rate of sexual dysfunction is low.

### Tricyclic antidepressants (TCA)

<table>
<thead>
<tr>
<th>Indications</th>
<th>Contraindications</th>
<th>Mechanism of action</th>
<th>Side effects</th>
<th>Examples</th>
</tr>
</thead>
<tbody>
<tr>
<td>TCA is an old antidepressant and it is not first-line antidepressant treatment due to potential cardiotoxicity if patient takes an overdose. Depression Anxiety disorder Severe OCD (Clomipramine) Neuropathic pain Migraine prophylaxis Enuresis</td>
<td>Cardiac diseases (e.g. post myocardial infarction, arrhythmias) Epilepsy Severe liver disease Prostate hypertrophy Mania</td>
<td>TCA inhibits the reuptake of both serotonin and noradrenaline and increase the concentration of these neurotransmitters. TCA also blocks histaminergic H1, α-adrenergic and cholinergic muscarinic receptors on the postsynaptic membrane.</td>
<td>Anticholinergic (e.g. constipation, blurred vision, urinary retention, dry mouth). dizziness, syncope, postural hypotension, sedation). Histaminergic and dopaminergic blockade: nausea, vomiting, weight gain, sedation, Other side effects: sexual dysfunction, hyponatraemia</td>
<td>Amitriptyline (25mg to 150mg daily) has the most potent anticholinergic effect. Clomipramine (100 – 225mg daily): Most potent TCA at D2 receptors; More selective inhibitor of serotonin reuptake.</td>
</tr>
</tbody>
</table>
Monoamine oxidase inhibitors (MAOIs)

**Reversible MAOI – Moclobemide** (Dose range: 75mg to 225mg daily; $0.45 per 150mg tablet)

<table>
<thead>
<tr>
<th>Indications</th>
<th>Contraindications</th>
<th>Mechanism of action</th>
<th>Side effects</th>
</tr>
</thead>
<tbody>
<tr>
<td>Atypical depression</td>
<td>Acute confusional state.</td>
<td>Monoamine oxidase A acts on</td>
<td>Visual changes.</td>
</tr>
<tr>
<td>Depression with predominantly anxiety symptoms</td>
<td>Phaeochromocytoma.</td>
<td>• Noradrenaline</td>
<td>Headache.</td>
</tr>
<tr>
<td>(e.g. social anxiety)</td>
<td></td>
<td>• Serotonin</td>
<td>Dry mouth.</td>
</tr>
<tr>
<td>Hypochondriasis</td>
<td></td>
<td>• Dopamine</td>
<td>Dizziness.</td>
</tr>
<tr>
<td></td>
<td></td>
<td>• Tyramine</td>
<td>GI symptoms.</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
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</tr>
</tbody>
</table>

The old irreversible MAOIs may lead to hypertensive crisis with food containing tyramine. Irreversible MAOIs are seldom used nowadays. The following food should be avoided:
1) Alcohol: avoid Chianti wine and vermouth but red wine <120 ml has little risk.
2) Banana skin.
3) Bean curds especially fermented bean curds.
4) Cheeses (e.g. Mature Stilton) should be avoided but cream cheese and cottage cheese have low risk.
5) Caviar.
6) Extracts from meats & yeasts should be avoided but fresh meat and yeast.

**Other antidepressants**

**Bupropion [Wellbutrin]** (Dose range: 150-300mg/day; $1.6 / 150mg tablet)

Similar efficacy as SSRI but voluntary withdrawal in the US due to induction of seizure at doses if the daily dose is higher than 450mg/day.

Other indications include patients encountering SSRI induced sexual dysfunction, female depressed patients do not want weight gain from medication and smoking cessation.

**Pharmacodynamics:** blocking dopamine reuptake.

**Side effects:** agitation, tremor, insomnia, weight loss and seizure. Bupropion is not associated with sexual side effect.
**Electroconvulsive therapy (ECT)**

**Indications:**
1) Severe depressive disorder which does not respond to an adequate trial of antidepressants.
2) Life threatening depressive illness (e.g. high suicide risk).
3) Stupor or catatonia
4) Marked psychomotor retardation
5) Psychotic depression
6) Treatment resistant mania
7) Treatment resistant schizophrenia.

**Relative contraindications:**
1) Raised intracranial pressure
2) Myocardial infarction
3) Valvular heart diseases
4) Aneurysm
5) Recent stroke
6) Peptic ulcer.

**Mechanism of actions:**
1) Release of noradrenaline, serotonin, dopamine but reduction of acetylcholine release.
2) Increase in permeability of the blood-brain barrier.
3) Modulation of neurotransmitter receptors such as GABA or acetylcholine.

**Administration:**
1. Usually bilateral temporal ECTs for adults for 6 treatments (3 times a week).
2. Unilateral ECT is reserved for old patients with the risk of cognitive impairment.
3. Bilateral ECT is more effective than unilateral ECT.
4. An informed consent is required prior to the ECT. A second opinion from another consultant psychiatrist is required for patient who lacks capacity or in cases of patient under Mental Disorder and Treatment Act who refuses treatment.
5. ECT is given under general anaesthesia. Muscle relaxant is given to prevent muscular spasms.
6. Electric current generates a seizure for less than one minute.
7. Before ECT, avoid long acting benzodiazepine which will affect the duration of seizure.
8. After ECT, patient is recommended to continue antidepressant for at least 6 months.

**Side effects:**
Common side effects include headache, muscle pain, jaw pain, drowsiness, loss of recent memories (retrograde amnesia), anterograde amnesia (less common than retrograde amnesia), prolonged seizures (longer than 1 minute) and confusion after ECTs.

Other side effects include anaesthesia complications arrhythmia, pulmonary embolism and aspiration pneumonia.

Factors increase seizure threshold: old age, male gender, baldness, Paget’s disease, dehydration, previous ECT and benzodiazepine treatment.
Factors decrease seizure threshold: caffeine, low CO\(_2\) saturation of blood, hyperventilation and theophylline.
OSCE video – Explain ECT (Refer to Clinical OSCE Videos)

You are the resident and you have admitted an elderly woman suffering from severe depressive episode with delusion of guilt. She does not respond to the antidepressant and antipsychotic drug. Your consultant has recommended ECT and her daughter is very concerned and wants to speak to you.

Task: Talk to her daughter and address her concerns.

- **Approach:** Express empathy. (e.g. I can imagine the idea of ECT sounds very scary for you, and it’s clear you want the best care for your mother. I would like to discuss what ECT involves, because it is very different than what is portrayed in the media. This way, you can make an informed decision)

- **Core information about ECT:**
  - ECT involves inducing a fit, while the patient is under general anaesthesia.
  - ECT is the most effective treatment for depression, particularly for those who have high risk of suicide, very poor appetite and not responding to oral medication; sometimes in pregnant women because it has no side effects to the foetus.
  - It is very safe and has been with us for the past 50 years.
  - **Will my mother be awake during ECT?** No, your mother will be given anaesthesia to put her into sleep and a medication that paralyze muscles, so the risk of breaking bones is rare. The patient is given oxygen before the procedure. The patient’s blood pressure, heart rhythm, and medical status is monitored throughout the procedure and when she comes out of the anaesthesia.
  - **How often will my mother get ECT and for how long?** 3 times per week, Mon, Wed, Fri and for 6 sessions (2 weeks); some patients may need 9 to 12 sessions.
  - **How do you know the ECT is successful or not?** We will monitor the duration of her fit. It has to be at least 25 second in duration. We will monitor her muscle movement through electrical recordings (i.e. EEG). If response is poor, we will increase the energy level 5% each time.
  - **How do you decide on the dose of ECT?** By age-based dosing: Energy level = patient’s age divided by 2.
  - **What tests do you include in your pre-ECT work-up?** Physical exam, FBC, RFT, ECG, CXR. Assess patient’s dentition, especially for elderly or those who have inadequate dental care.
  - **What is the preparation for the night before the ECT?** Fasting is required after 12:00 midnight and she should avoid sleeping pills if possible.
  - **What is the risk involved?** ECT itself is safe. Risk is associated with anaesthesia.
  - **How does ECT affect memory?**
    - Anterograde and retrograde amnesia can occur, though in the majority of patients this does not last more than a few months following the last ECT treatment.
    - Amnesia of events immediately preceding and following ECT treatments may be permanent (reassure the relative those memory is not important).
    - Anterograde amnesia is always transient. In a very small number of patients, the symptoms of retrograde amnesia may be permanent.
  - **What are other common side effects?** Memory problems, confusion, nausea, muscle aches and headache are the most common in the morning after the ECT.
  - **What are the risk factors associated with confusion after ECT?** Old age; prior cognitive impairment; lithium; anticholinergic and bilateral placement.
  - **How would you reduce confusion after ECT?** Unilateral treatment on right – side of the brain, lower electrical energy, increasing the time between ECT treatments and holding off lithium or sleeping pills.
  - **What is the mortality rate associated with ECT?** The mortality rate is very low, and is the same as that for general anaesthesia, which is 1 in every 20,000 people.

Psychotherapy

1. **Cognitive behaviour therapy (CBT).** The frequency of CBT is usually weekly or fortnightly. It requires 12 to 16 sessions. The cognitive therapy involves identifying negative automatic thoughts and use dysfunctional thought diary to identify pattern between the time, events, negative thoughts and resulted emotions and behaviours. The psychologist will read the diary and help patients to gently challenge the negative automatic thoughts. Behaviour therapy involves activity scheduling (for those depressed patients with psychomotor retardation), relaxation techniques (for those patients with mixed anxiety and depression).
2. **Interpersonal therapy (IPT)** IPT is held weekly or fortnightly. It involves 12 to 20 sessions. IPT is indicated for depressed patients whom precipitating factor is interpersonal problems. The psychologist closely examines interpersonal relationship and works with the patient to look at interpersonal relationship from another angle to minimise impact on the mood and use role-play to improve communication skills.

3. **Brief dynamic therapy** Brief dynamic therapy originates from psychoanalysis. Brief dynamic therapy is suitable for depressed patients whose predisposing factor is related to past experiences (e.g. unpleasant childhood experience with one of the parents) and these experiences have lead to the use of maladaptive defence mechanisms and affect current mood and personality development. Brief dynamic psychotherapy is contraindicated in psychotic patients.

4. Other psychotherapies include supportive psychotherapy, problem solving therapy or marital therapy depending on clinical history and case formulation.

### Course and prognosis

- Depressive episodes may last from 4-30 weeks for mild or moderate depressive disorder to an average of around 6 months for severe depressive disorder.
- 10-20% of patients would have depression as a chronic disorder, with signs and symptoms lasting for around 2 years.
- The rate of recurrence is around 30% at 10 years and around 60% at 20 years.
- Suicide rates for depressive individuals is 20% higher when compared to the general population.
- Good prognostic factors include acute onset of depressive illness, endogenous depression and earlier age of onset. Poor prognostic factors include insidious onset, old age of onset, neurotic depression, low self-esteem and residual symptoms.
Bipolar disorders

Epidemiology

<table>
<thead>
<tr>
<th></th>
<th>Prevalence</th>
<th>Mean age of onset</th>
<th>Gender ratio</th>
</tr>
</thead>
<tbody>
<tr>
<td>International</td>
<td>0.3 – 1.5% (overall)</td>
<td>20 years.</td>
<td>Male: female = 1:1.</td>
</tr>
<tr>
<td></td>
<td>0.2 – 4% (Bipolar I disorder)</td>
<td></td>
<td></td>
</tr>
<tr>
<td></td>
<td>0.3 – 4.8% (Bipolar II disorder).</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Aetiology

Genetics:
- Family studies have demonstrated that children of parents suffering from bipolar disorder have a 9-fold increase in lifetime risk compared to the general population.
- The heritability of bipolar disorder is 79-93%
- Twin studies indicate that monozygotic twins have 70% concordance rate and dizygotic twins have 20% concordance rate.
- Genes related to ion channels are implicated in the aetiology of bipolar disorder (e.g. calcium channels on chromosome 12). (Ferreira et al, 2008).

Monoamine theory states that increased levels of noradrenaline, serotonin and dopamine have been linked with manic symptoms. Excitatory neurotransmitter glutamate is also implicated.

The onset and first manic episode: The diagnosis is commonly delayed until early adulthood (median age of onset is in mid-20s and mean age of first hospitalisation is at 26 years) because there is abnormal programmed cell death or apoptosis in neural networks responsible for emotional regulation. The first manic episodes are often precipitated by life events such as bereavement, personal separation, work-related problems or loss of role. High expressed emotion and sleep deprivation are important precipitating factors.

The relationship between depressive and manic episodes: 1 in 10 patients who suffer from a depressive episode will subsequently develop a manic episode. Monotherapy of antidepressant is a recognised precipitant of the first manic episode in patients who are predisposed to suffer from bipolar disorder. In general, depressed patients with early age of onset, family history of bipolar disorder, depressive episode occurring during postnatal period, hypersomnialia and psychotic symptoms are more likely to switch to mania.

Sleep deprivation and flying overnight from west to east may trigger relapse of mania.

Kindling hypothesis: The persistence of neuronal damage leads to recurrence of mania without precipitating factors. This is known as kindling and subsequent manic episodes become more frequent. The episode duration remains stable throughout the course of bipolar illness.
Organic causes of mania

Cerebrovascular accident
Mania is associated with right-sided cerebral vascular lesions and it is commonly associated with lesions in the frontal and temporal lobes.

Head injury
Mania is associated with right-sided hemispheric damage. Family history of mania is uncommon and patients are more irritable than euphoric.

Other CNS disorders
1. Cerebral tumour
2. Dementia
3. Epilepsy
4. AIDS
5. Multiple sclerosis

Endocrine causes
1. Thyrotoxicosis
2. Thyroid hormone replacement
3. Cushing’s syndrome

Illicit substances:
1. Amphetamine
2. Cannabis
3. Cocaine

Medications:
1. Anticholinergic drugs
2. Dopamine agonists (e.g. bromocriptine and levodopa)
3. Corticosteroids or anabolic steroids
4. Withdrawal from baclofen, clonidine and fenfluramine.

Lesions in right cerebral hemisphere are associated with mania
Diagnostic criteria for bipolar disorder (RATA)

**Appearance**
- Increased sociability or over-familiarity

**Thoughts**
1. Difficulty in concentration with distractibility
2. Flight of ideas or racing thought (In ICD-10, this only occurs in mania but not hypomania)
3. Inflated self esteem and grandiosity (In ICD-10, this only occurs in mania but not hypomania)
4. Constant change in plans (In ICD-10, this only occurs in mania but not hypomania)

**Affect:**
- Elevation of mood and irritability

**Hallucination**
- Mood congruent: voices telling the patient that he has superhuman powers.
- Mood incongruent: voices speaking to the patients about affectively neutral subjects.

**Interest**
- Increase in goal – directed activity (either socially, at work or school or sexually) or excessive involvement in pleasurable activity that have a high potential for painful consequences (e.g. unrestrained buying sprees, sexual indiscretion or foolish business)

**Speech**
- Increased talkativeness

**Reality axis**

**Mania**

**Delusion**
- Mood congruent: grandiose delusions
- Mood incongruent: delusion of reference and persecution

**Behaviour**
- Increased activity and physical restlessness
- Decreased need for sleep
- Increased sexual energy (hypomania) / Sexual indiscretions (mania)
- Mild overspending or other types of reckless or irresponsible behaviour (hypomania)/Foolhardy and reckless behaviour with lack of awareness (mania)
- Loss of social inhibition, resulting in inappropriate behaviour

Compare and contract ICD-10 and DSM-IV-TR criteria for bipolar disorder

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>ICD-10</th>
<th>DSM-IV-TR</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Bipolar I and II</strong></td>
<td>Not stated</td>
<td>Bipolar I disorder is associated with manic episodes. Bipolar II disorder is associated with hypomanic episodes.</td>
</tr>
<tr>
<td><strong>Hypomania</strong></td>
<td>The duration is of several days. ICD-10 has listed specific diagnostic criteria found in mania but not hypomania (see below).</td>
<td>At least 4 -day duration and at least 3 cognitive or biological symptoms. Associated with inflated self esteem and grandiosity, flight of idea, increase in goal – directed activity (either socially, at work or school or sexually)</td>
</tr>
<tr>
<td><strong>Mania</strong></td>
<td>The following symptoms occur in mania but not hypomania. 1. Flight of ideas or racing thought. 2. Inflated self esteem and grandiosity. 3. Constant change in plans. 4. Sexual indiscretions. 5. Foolhardy behaviour. 6. Psychotic features.</td>
<td>At least 1 week duration and at least 3 cognitive or biological symptoms.</td>
</tr>
<tr>
<td><strong>Mixed episode and rapid</strong></td>
<td>For mixed affective episode, patient exhibits mixed affective symptoms. Both manic and depressive symptoms must be present for greater</td>
<td>Mixed episodes refer only to patients fulfil both mania and major depression for at least 1 week. Rapid cycling as a course of bipolar disorder which</td>
</tr>
<tr>
<td>cycling disorders</td>
<td>part of the current episode and symptoms can rapidly alternate.</td>
<td>consists of at least 4 episodes of mood disturbance (manic, hypomanic and major depressive episode) in one year. Ultra-rapid cycling describes 4 or more episodes in a month and it is a rare condition. Note: Rapid cycling is more common in women, occurring later in the course of bipolar illness and antidepressants can increase the frequency of rapid cycling episodes.</td>
</tr>
</tbody>
</table>

**OSCE grid: Assess bipolar disorder**

You have been asked to see a 28-year-old unemployed man who has not slept for 5 days and claims to have full energy. He claims to be the President of Singapore and his plan is to unite all the world leaders to fight for poverty in developing countries.

**Task:** Take a history to establish the diagnosis of bipolar disorder.

| | | | | Do you feel that they annoy you? |
| | | If I ask you to rate your mood from 1 to 10, 1 means very depressed and 10 means very happy, how would you rate your mood today? | | Do you lose your temper easily? |
| | | How long have you been feeling high? | | What would you do if these people irritate you? |
| | | Do you have mood swings? How about feeling low? If so, roughly how many low or high episodes you would experience in a year? | | |

| | | What is your energy level like? | | Have you lost weight recently? |
| | | Do you feel that you need much less sleep but full of energy? | | |

| C. Assess cognitive and psychotic symptoms. | C1. Assess interests and plans. | Could you tell me about your interests? | C2. Assess thought and speech. | Has there been any change in your thinking lately? |
| | | Have you developed any new interests lately? | | Have you noticed that your thoughts speed up? |
| | | Do you have any new plan or commitment at this moment? (for | Do you find your thoughts |
| | | | | |
| | | | | |

| A3. Assess grandiosity | How would you compare yourself with other people? | |
| | Are you special? If yes, please tell me more. | |
| | Could your special ability be a misunderstanding? Can you provide more evidence about it? | |
| | Do you feel that you are at the top of the world (i.e. above all the other people)? | |
example, starting a new business or investment) racing in your mind? Do your family members say that the topics in your speech change so fast and they cannot follow. many voices spoke at one time? Do you believe that you have special power or status which other people do not have? If yes, can you tell me about your special power or status? Are you very certain that you have such ability or status?

D. Assess risk and insight

D1. Assess risk.
Have you been buying a lot of things? Have you incurred a lot of debts (e.g. credit card debts?)
Do you drive? Have you been involved in speeding or traffic offences?
Have you been in trouble with the police lately? (e.g. due to violence).
When you feel sad, have you thought of harming yourself?

D2. Explore comorbidity.
Do you take recreational drugs on a regular basis to get the high feelings?
How about alcohol? Do you drink on a regular basis?

D3. Assess insight.
Is there any reason why you encounter those experiences?
Do you think there is an illness in your mind? For example, this illness affects your mood?
If so, do you think you need treatment?

Investigations and questionnaire
- FBC, ESR.
- LFT, RFT, TFT, fasting lipid, glucose and body weight measurement (as mood stabilisers are associated with metabolic syndrome).
- VDRL.
- Urine drug screen
  - Pregnancy test (for female patients who may be pregnant).
- CT/MRI to rule out space occupying lesion, infarction, haemorrhage.
- ECG to rule out prolonged QTc.
- EEG to rule out epilepsy.

The Young mania rating scale (YMRS)

The YMRS is an 11-item questionnaire which helps clinicians to measure the severity of manic episodes in children and adolescents between the ages of 5 and 17 and adults. Its structure is similar to the Hamilton depression scale.

Management

Summary of MOH guidelines (Mok et al 2011) and NICE guidelines (UK)

| Acute treatment of mania | Hospitalisation may be necessary in patients present with severe manic symptoms or pose serious risk e.g. violence, sexual indiscretions). Some manic patients who refuse treatment may require |
admission under the Mental Disorder and Treatment Act.

Haloperidol may be used for the treatment of acute mania.

Aripiprazole, olanzapine, quetiapine, risperidone or ziprasidone may be used for the treatment of acute mania.

Sodium valproate or carbamazepine monotherapy may be used for the treatment of acute mania.

Lamotrigine should not be used for the treatment of acute mania, as it lacks efficacy in this area.

Combination pharmacotherapy with an antipsychotic and a mood stabiliser may be used for patients showing inadequate response to mood stabiliser monotherapy.

Clonazepam or lorazepam (IM or oral) may be used in the acute treatment of agitation in mania.

In the emergency setting, Haloperidol (IM or oral) or olanzapine (oral) may be used in the acute treatment of agitation in mania.

<table>
<thead>
<tr>
<th>Acute treatment of bipolar depression.</th>
<th>For mild depressive symptoms, it is recommended to review patients in 1 to 2 weeks without giving an antidepressant.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>If depressive symptoms are moderate to severe, consider adding antidepressant to a mood stabiliser.</td>
</tr>
<tr>
<td></td>
<td>If antidepressants are to be used in combination with mood stabilisers as treatment for bipolar depression, they should be used cautiously due to conflicting evidence of efficacy and risk of inducing a manic episode. SSRI such as fluoxetine is the first line of treatment.</td>
</tr>
<tr>
<td></td>
<td>Lithium may be used in the treatment of bipolar depression.</td>
</tr>
<tr>
<td></td>
<td>Quetiapine monotherapy, olanzapine monotherapy or olanzapine-fluoxetine combination may be used in the treatment of bipolar depression.</td>
</tr>
<tr>
<td></td>
<td>Monotherapy with sodium valproate or carbamazepine is not recommended in the treatment of bipolar depression due to conflicting evidence regarding efficacy.</td>
</tr>
<tr>
<td></td>
<td>There is insufficient evidence to recommend lamotrigine monotherapy in the treatment of bipolar depression. However, it is recommended as an add-on for patients already on lithium for treatment of bipolar depression.</td>
</tr>
<tr>
<td></td>
<td>Psychotherapy (e.g. CBT) is recommended for patients with bipolar depression.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Rapid cycling and mixed state.</th>
<th>Mood stabilisers may be used when treating mixed states. Of these, valproate and carbamazepine should be preferred over lithium, as there is more evidence for the efficacy of valproate and carbamazepine than for lithium.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Non-pharmacological treatments should not be used for patients with rapid cycling bipolar disorder due to insufficient evidence.</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Maintenance treatment</th>
<th>Lithium, valproate or olanzapine may be used as maintenance therapy in preventing relapse to either pole of illness in patients with bipolar disorder.</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Aripiprazole may be used as maintenance therapy in bipolar patients with recent manic or mixed episode.</td>
</tr>
<tr>
<td></td>
<td>Quetiapine, in combination with lithium or valproate, may be used as maintenance therapy in</td>
</tr>
</tbody>
</table>
patients with bipolar I disorder.

In very severe patients, the combination of lithium and valproate is possible and this should be a specialist’s decision.

A patient is advised to continue treatment for at least 2 years after an episode of bipolar disorder and up to 5 years if there is a significant risk of relapse.

<table>
<thead>
<tr>
<th>Bipolar disorder and pregnancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Typical antipsychotics, such as chlorpromazine and haloperidol, may be considered for treatment of pregnant women with bipolar disorder, as they appear less likely than atypical antipsychotics to cause metabolic complications and other serious adverse effects.</td>
</tr>
<tr>
<td>Electroconvulsive therapy may be considered as a treatment option in pregnancy for the same indications as in nonpregnant patients.</td>
</tr>
<tr>
<td>Women on combined oral contraceptive pills who are concurrently taking carbamazepine and/or lamotrigine should be advised of the risk of decreased contraceptive effect as a result of drug interactions.</td>
</tr>
<tr>
<td>Lithium may cause Ebstein’s abnormality in the foetus’ hearts.</td>
</tr>
<tr>
<td>Use of sodium valproate in women of childbearing age should be balanced against the risk of decreased fertility, foetal malformations and perinatal complications. Sodium valproate may cause polycystic ovary syndrome and reduce the chance of pregnancy. Sodium valproate may cause neural tube defects in foetuses. Periconceptional folate supplementation should be prescribed to protect against neural tube defects.</td>
</tr>
<tr>
<td>For pregnant women with bipolar disorder, consider switching to antipsychotic treatment, or gradual decrement (over 15–30 days) of monotherapy mood stabiliser to the lowest effective amount in divided doses during pregnancy. Concurrent careful foetal monitoring is recommended.</td>
</tr>
<tr>
<td>Sodium valproate and carbamazepine are preferable to lithium and lamotrigine during Breastfeeding. Mothers who require the latter two medications may be advised to consider abstinence from breastfeeding for the infant’s safety.</td>
</tr>
<tr>
<td>In the event of breastfeeding while taking mood stabilisers, consider administering feeds before taking medication and discarding the first post-dose batch of expressed milk, so as to minimise the infant’s consumption of medication via breast milk.</td>
</tr>
</tbody>
</table>

**Mood stabilisers**

**Compare and contrast mood stabilisers:**

|---------|------------------------------------|--------------------------------|------------------------|

*Mastering Psychiatry – A Core Textbook for Undergraduates*
<table>
<thead>
<tr>
<th><strong>Dose:</strong> Oral, start at 400mg. Maximum 1200mg per day. Lithium carbonate CR: $0.38 / 400mg tablet.</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Dose:</strong> Oral, starts with 500mg daily, Maximum 1300mg per day. $0.5 per 300 mg tablet.</td>
</tr>
<tr>
<td><strong>Dose:</strong> 400mg – 800mg Carbamazepine CR $0.16 / 400mg tablet.</td>
</tr>
<tr>
<td>A slow titration is required and this will avoid a serious skin rash: 25 mg/day for 2 weeks doubling the dose every two weeks to a maximum of 400 mg/day. $1.09 / 50mg tablet $1.72 / 100mg tablet</td>
</tr>
</tbody>
</table>

**Monitoring:**
- Lithium level should be checked every 3 months. (0.4 – 0.8 mmol/L: maintenance range.
- RFT is checked every 6 months.
- TFT is checked every year.
- LFT is a must before starting a patient on sodium valproate.

**Properties:**
- Remains a first line treatment in bipolar disorder.
- Lithium increases Na/K/ATP-ase activity in patients. It affects serotonin, noradrenaline, dopamine and acetylcholine. Lithium also interferes cAMP (second messenger system).
- Onset of action: 5-14 days.
- Anti-mania effect is proportional to plasma levels. The level is set to be between 0.4 – 0.8 mEq/L for Asian patients.
- Lithium is often used with antidepressants and other mood stabilizers in bipolar depression.
- Lithium reduces suicidal ideation in bipolar patients.
- Efficacy is superior to placebo but equal to lithium, haloperidol, and olanzapine.
- Valproate enhances GABA function and produces neuroinhibitory effects on mania.
  - Valproate can be combined with antipsychotics in treatment of mania and lower dose of antipsychotic drug is required.
  - Valproate is effective in maintenance treatment to prevent mood episodes.
  - Effective plasma levels: 50-99 mg/L but clinical response is more important.
- Valproate is indicated in patients with renal failure and rapid cycling disorder but contraindicated in people with liver failure.
- The application of carbamazepine is limited by its properties as an enzyme inducers and side effects such as diplopia, blurred vision, ataxia, somnolence, fatigue, nausea, and blood dyscrasia.
- Generally effective in maintenance treatment to prevent mood episodes.
- No data on plasma levels and response.
- Carbamazepine is indicated to patients with bipolar disorder who are concerned about weight gain caused by lithium and valproate because carbamazepine does not cause significant weight gain.

**Side effects:**
- Common side effects:
- Common side effects:
- Common side effects:
Common side effects:
- Metallic taste
- Nausea
- Polydipsia
- Polyuria
- Oedema
- Weight gain
- Fine tremors.

Long term complications:
- Hypothyroidism
- Renal failure

Weight gain
Nausea
Gastric irritation
Diarrhoea
Serious side effect:
Thrombocytopenia.

Dizziness
Somnolence
Nausea
Dry mouth
Oedema
Hyponatraemia (due to potentiation of ADH)
↑ALP and ↑GGT.

Uncommon side effects:
- Ataxia
- Diplopia
- Nystagmus
- Serious exfoliative dermatological reactions (3% of patients and requires cessation of carbamazepine.
- Agranulocytosis
- Leucopenia
- Aplastic anaemia.

Dizziness
Headache
Diplopia
Nausea
Ataxia.

Uncommon side effects
If patients develop for lamotrigine-associated rash (10%), hold the next dose and seek immediate medical attention.

Lithium toxicity

<table>
<thead>
<tr>
<th>Lithium level</th>
<th>Signs of lithium toxicity</th>
</tr>
</thead>
<tbody>
<tr>
<td>1.5 – 2.0 mmol/L</td>
<td>CNS: Drowsiness, malaise and poor concentration. Toxic signs in CNS does not closely follow</td>
</tr>
<tr>
<td></td>
<td>changes in lithium blood levels. PNS: Muscle weakness and severe fine tremor. GIT: Anorexia</td>
</tr>
<tr>
<td></td>
<td>and diarrhoea which resemble gastroenteritis.</td>
</tr>
<tr>
<td>(Mild toxicity)</td>
<td></td>
</tr>
<tr>
<td>2.0 -3.0 mmol/L</td>
<td>CNS: Disorientation and dysarthria. CV: Cardiac arrhythmia. PNS: Coarse tremor, restless</td>
</tr>
<tr>
<td>(Moderate toxicity)</td>
<td>and ataxia. GIT: Vomiting.</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 3.0 mmol/L</td>
<td>CNS: Confusion and convulsion and coma. CV: Cardiovascular collapse. Respiratory: Severe</td>
</tr>
<tr>
<td>(Severe toxicity)</td>
<td>viscosity of respiratory secretions. Haemodialysis may be necessary when serum levels exceed 3mmol/L.</td>
</tr>
<tr>
<td></td>
<td></td>
</tr>
<tr>
<td>&gt; 5.0 mmol/L</td>
<td>It may lead to permanent physical damage and mortality.</td>
</tr>
</tbody>
</table>

Treatment of lithium toxicity involves cessation of lithium and dialysis.

OSCE video – Explain lithium and side effects

A patient was admitted to the psychiatric ward after a manic episode. The consultant psychiatrist has advised him to consider taking lithium as a maintenance treatment. The patient is very concerned about bipolar disorder and lithium after reading the information from internet.

Task: address his concerns about lithium treatment.

1. **Why do you want to prescribe lithium?** Lithium is used to stabilise your mood. After my assessment, your mood seems to be elevated and you suffer from a condition called mania in the context of bipolar disorder.

2. **What is mania?** Feeling high, irritable, full of energy, very good appetite, no need for sleep, high sexual drive,
racing thoughts, grandiose ideas, overspending, poor judgement, dangerous behaviour and unusual experiences such as hearing voices.

3. Why do I sometimes feel depressed? Periods of depression occur in bipolar disorder. Your mood will go up and down.

4. What exactly is lithium? It is a type of salt and can be found naturally.

5. How long have psychiatrists been using lithium? 50 years already.

6. What is the usual dose of lithium? Starting dose 400mg a day, increase slowly to 800mg to 1200mg per day.

7. How do you decide the right dose for me? Based on serum levels 0.4 – 0.8 mmol/L; clinical response.

8. What time of the day should I take lithium? Usually at night. The modern lithium has long release version and can last for whole day.

9. What should I do if I miss a dose? If you forget a dose, take it ASAP as you remember.

10. Can I take lithium now? No, we need to do some blood tests for you.

11. What do you need those blood tests? To check it is safe for you to take lithium. Your kidney and thyroid have to be in good condition.

12. Do I only need to have those blood tests once? The lithium may affect the function of kidney and thyroid. We have to check every 6 months.

13. Lithium sounds scary. How do you know it is safe for me to take? It is usually safe if your kidney and thyroid are in good condition. Extra care if you take pain killer, medication containing sodium.

14. How do I know lithium works for me? Your highs and lows become less extreme. It will reduce thoughts of harming oneself. It may take weeks or months to appreciate the beneficial effects of lithium.

15. Can I mix alcohol with lithium? No, it will lead to drowsiness if lithium combines with alcohol, ↑ fall risk & accidents. Avoid alcohol in 1st & 2nd months; if you need to drink socially, try a small amount & see how you feel. Don’t drink and take lithium when you drive.

16. When I feel better, can I stop taking lithium? You should not stop suddenly. Need to consult your doctor. Lithium is usually a long-term treatment.

17. Is lithium addictive? No, it is because you do not need to take more and more lithium to achieve the same effect.

18. Do I need to know anything else as I stay in Singapore? Drink enough water in hot weather. Lack of water in body may cause more side effects.

19. My younger brother likes to steal my medicine. What would happen to him if he swallows a large amount of lithium? Lithium is toxic if a person takes an overdose. A person will first present with loose stool/vomiting, then very shaky hands, unsteady walking, confusion and may die. You need to send the person to the Emergency Department immediately.

20. What are the other alternatives besides lithium? There are other medications which can stabilise patient’s mood which are anti-fit / epilepsy medication.

**Non-pharmacological treatment**

- **Cognitive therapy** to challenge grandiose thoughts.
- **Behaviour therapy** to maintain regular pattern of daily activities.
- **Psychoeducation** on aetiology, signs and symptoms, management and relapse prevention of bipolar disorder.
- **Family therapy**: To work on impact of manic symptoms on family and resolve interpersonal problems.
- **Relapse drills**: to identify symptoms and to formulate a plan to seek help in early manic phase..

**Course and prognosis**

- Manic episodes usually last between 2 weeks to 4 months. Depressive episodes usually last for 6 months.
- Length of time between subsequent episodes may begin to narrow and remission time decreases with increasing age.
- Lithium can bring 60-70% remission rate.
- Good prognostic factors: female gender, short duration of manic episode, later age of onset, no suicidal thoughts, less psychotic symptoms, few comorbid physical conditions and good compliance.
- Poor prognostic factors include male gender, long duration of manic episode, early age of onset, suicidal thought, depressive symptoms, psychotic symptoms, comorbidity (e.g. alcohol or drug misuse) and poor compliance.

**Suicide and deliberate self harm**

<table>
<thead>
<tr>
<th>Epidemiology [Chia BH, 2010]</th>
<th>Suicide</th>
<th>Deliberate self harm</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Male : Female = 3:1.</td>
<td>• More common in women</td>
<td></td>
</tr>
<tr>
<td>• More common in older people.</td>
<td>• Most common in adolescents</td>
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</tbody>
</table>
Suicide rates in Singapore remained stable between 9.8-13.0/100,000 from 1955 to 2004. Rates remain highest in elderly men. Rates in ethnic Chinese and Indians were consistently higher than in Malays. The rates among female Indians and Chinese have declined significantly between 1995 and 2004, some increase was noted in female Malays.

It is estimated that 7-14% of adolescents have self-harmed (UK).

Common methods used in Singapore between 2000 and 2004 were jumping (72.4%), hanging (16.6%), and poisoning (5.9%) [Chia et al 2011].

Types of self harm include: cutting usually of the wrists or forearms, scratching, burning skin or banging the head against the wall.

**Questionnaire to assess suicide risk – The SAD PERSONS assessment tool [Patternson et al 1983].**

<table>
<thead>
<tr>
<th>Item</th>
<th>Score</th>
<th>Item</th>
<th>Score</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex = Male.</td>
<td>1</td>
<td>Psychosis.</td>
<td>2</td>
</tr>
<tr>
<td>Age &lt; 19 or &gt; 45.</td>
<td>1</td>
<td>Separated/widowed/divorced.</td>
<td>1</td>
</tr>
<tr>
<td>Depression or hopelessness.</td>
<td>1</td>
<td>Serious attempt (e.g. hanging, stabbing).</td>
<td>2</td>
</tr>
<tr>
<td>Previous suicide attempts.</td>
<td>1</td>
<td>No social support.</td>
<td>1</td>
</tr>
<tr>
<td>Excessive alcohol or drug use.</td>
<td>1</td>
<td>Stated future intent.</td>
<td>2</td>
</tr>
</tbody>
</table>

Total score < 6 (may be safe to discharge); 6-8 (refer to psychiatric assessment) and > 8 = urgent admission.

**CASC grid – Assess suicide risk**

A 24-year-old woman took an overdose of 20 tablets of paracetamol. She is brought in by her partner to the Accident and Emergency Department and you are the resident on duty at the Accident and Emergency Department.
### Task: Assess her suicide risk.

<table>
<thead>
<tr>
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<tbody>
<tr>
<td>I am Dr. XXX. I can imagine that you have gone through some difficult experiences. Can you tell me more about it?</td>
<td>Was the overdose planned? If yes, how long have you thought about it?</td>
<td>Have you thought about taking your own life by the overdose?</td>
<td></td>
</tr>
<tr>
<td>Can you tell me why you took the 20 tablets of paracetamol tonight?</td>
<td>How did you collect the paracetamol tablets?</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Was there any life event leading to this suicide attempt?</td>
<td>What did you think would happen when you took the paracetamol?</td>
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<tbody>
<tr>
<td>Where did you take the medication?</td>
<td>Besides the paracetamol, did you take other tablets?</td>
<td>Did you mix the paracetamol with alcohol?</td>
<td>Was a suicidal note left?</td>
</tr>
<tr>
<td>Was anyone else there/were you likely to be found?</td>
<td>Did you harm yourself by other means? (e.g. cutting yourself)</td>
<td>Did you send a SMS or email to say ‘good-bye’ to your partner or family members?</td>
<td></td>
</tr>
<tr>
<td>Did you lock the door or take precaution to avoid discovery?</td>
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</thead>
<tbody>
<tr>
<td>How did you come to be in A&amp;E?</td>
<td>Did the overdose lead to any discomfort? E.g. severe vomiting.</td>
<td>How do you feel about it now?</td>
<td></td>
</tr>
<tr>
<td>Were you discovered by other people? If yes, how did they discover you?</td>
<td>Did you have a period of blackout?</td>
<td>Are you regretful of your suicide attempt?</td>
<td></td>
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</thead>
<tbody>
<tr>
<td>Have you attempted suicide previously?</td>
<td>Do you have a history of mental illness? (e.g. depression) and take a brief mood history and past treatment if depression is present.</td>
<td>We have discussed quite a lot on the overdose and some of the unhappy events. Are there things in life you are looking forward to?</td>
<td></td>
</tr>
<tr>
<td>If yes, how many times?</td>
<td>Are you suffering from any other illnesses? (e.g. chronic pain)</td>
<td>Who are the people supporting you at this moment?</td>
<td></td>
</tr>
<tr>
<td>What are the usual causes of suicide attempts?</td>
<td></td>
<td>How about religion?</td>
<td></td>
</tr>
<tr>
<td>Did you try other methods like hanging, stabbing yourself, jumping from heights or drowning?</td>
<td></td>
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</tr>
</tbody>
</table>

**Bereavement and abnormal grief**
Grief and depression

Bereavement

- **Phase I: Shock and protest** includes numbness, disbelief and acute dysphoria.

- **Phase II: Preoccupation** includes yearning, searching and anger.

- **Phase III Disorganization** includes despair and acceptance of loss.

- **Phase IV: Resolution**

  e.g. On Christmas day, a 64-year-old woman was brought to the emergency department as she suddenly becomes tearful and starts hitting herself. On further enquiry, her daughter was killed in a road traffic accident on the Christmas eve 2 years ago.

**Pathological Grief**

- **Inhibited grief**: absence of expected grief symptoms at any stage.

- **Delayed grief**: avoidance of painful symptoms within 2 weeks of loss.

- **Chronic grief**: continued significant grief related symptoms 6 months after loss.

**Depressive episode**

A person may undergo depression after bereavement. The following features suggest depression rather than bereavement:

- Guilt, suicidal thoughts & hallucinations not related to the deceased.

- Feelings of worthlessness.

- Psychomotor retardation.

- Prolonged and marked functional impairment.

**Management for abnormal grief**: Grief therapy which focuses on talking about the deceased, prepare for future life without the deceased, plan to discard items related to the deceased and have a closure of unresolved issues related to the deceased.

**Seasonal affective disorder (SAD)**

**Definition**: SAD is a form of recurrent depressive disorder, in which sufferers consistently experience low mood in winter months. Symptoms include increase appetite, craving for sugar or rice, low energy, increased sleep and weight gain.

**Worst months**: November & December in Europe; January & February in US.

**Aetiology**: 1) melatonin/pineal gland abnormalities, replaced by theories on disordered brain 5HT regulation, phase-advanced circadian rhythms. 2) Biologically vulnerable individuals is affected by the actual effect of the changes in the seasons and specific anniversary or environmental factors in winter.

**Epidemiology**: 3% in Europe

**Clinical features**: SAD presents with features of atypical depression – hypersomnia, hyperphagia, tiredness and low mood in winter. ICD-10 criteria specifies 3 or more episodes of mood disorder must occur with onset within the same 90-day period of the year for 3 or more consecutive days. Remission also occurs within a particular 90-day period of the year. Seasonal episodes substantially outnumber any non-seasonal episodes that may occur.

**Treatment**: Light therapy involves a special light box which emits 2500 lux and mimics the effect of sunlight for at least 2 hours every morning (or 10000 lux for 30 minutes). Exposure to eyes is important as it alters circadian rhythm. Effects are seen within a few days but it takes 2 weeks for the full effect. The person should use the light box half an hour a day starting in autumn & throughout winter months to prevent relapse. Melatonin levels are lowered with light therapy. 50% of people with SAD show clinically significant response to light therapy. Untreated episodes resolve by spring time. Side effects include jumpiness, headache & nausea (15% of patients) Other treatment includes sleep deprivation.

**Revision MCQs**

1. A mother worries that her daughter will develop depression because of the family history of depressive disorder. Which of the following genes is associated with increased risk?
   - A. APO E4 gene on chromosome 21
   - B. COMT gene on chromosome 21
   - C. Presenilin-2 gene on chromosome 1
   - D. Presenilin-1 gene on chromosome 14
   - E. Serotonin transporter gene
The serotonin transporter gene is implicated in the aetiology of depressive disorder. Short allele (SS) variation in the promoter region of the 5-hydroxytryptamine transporter gene (5-HTTLPR) decreases the transcriptional efficacy of serotonin and cause major depressive disorder in response to stressful life events.

2. A 32-year-old woman suffers from a severe depressive episode. She has three young children studying in primary school. She is unemployed with no confiding relationship. Which of the following works provides an explanation in her case?
A. Brown and Harris: Social Origins of Depression
B. Durkheim E: Anomie
C. Habermas J: The Theory of Communicative Action
D. Parsons T: The Social System
E. Sullivan HS: The Interpersonal Theory of Psychiatry

Answer: A
G.W. Brown and T. Harris published the Social origins of depression: A study of psychiatric disorder in women in 1978. In this book, Brown and Harris stated that women with three young children under the age of 14, unemployed and with no confiding relationship are more likely to develop depression.

3. You are teaching depressive disorder to a group of medical students. They want to know what percentage of patients admitted to the university hospital will have recurrence and require further admission in long run without committing suicide. Your answer is:
A. 20%
B. 30%
C. 40%
D. 60%
E. 80%

Answer: D
An old British study showed that approximately 60% of patients had been re-admitted at least once. Only 20% had recovered fully with no further episodes and 20% were incapacitated throughout or died of suicide.

4. A 30-year-old woman suffers from depression with melancholic features. When compared with depressed patients without melancholia, which of the following statements is incorrect?
A. Cortisol is less likely to be suppressed when this patient is administered with dexamethasone suppression test
B. She is more likely to develop psychomotor retardation
C. She has greater symptom severity
D. She has increased REM latency
E. She has lower placebo response

Answer: D
Depressed patients with melancholic features have decreased REM latency.

5. A 40-year-old woman suffers from severe depressive episode with psychotic features. Which of the following statements is incorrect?
A. Mood incongruent psychotic features predict a better outcome
B. Psychotic symptoms must occur after manifestations of depressive symptoms
C. She has more biological abnormalities compared with depressed patients without psychotic features
D. She has poorer long-term outcome
E. She may be benefitted by receiving ECT

Answer: A
Mood incongruent psychotic features predict a poorer course and outcome.

6. A 23-year-old woman complains of hearing voices. A core trainee is not certain whether this patient suffers from schizophrenia or bipolar disorder. Which of the following features suggest the diagnosis of bipolar disorder rather than schizophrenia?
A. Bizarre delusions
B. Persecutory delusions
C. Prominent affective symptoms and mood congruent delusions
D. Systematized delusions
E. Thought broadcasting

Answer: C
Prominent affective symptoms and mood congruent delusions support the diagnosis of bipolar disorder.

7. A 30-year-old woman suffers from severe depressive episodes, but she tends to forget to take her medication at least twice a week. She finds it very difficult to take medication on a daily basis. She requests that you should prescribe an antidepressant which suits her needs. Which of the following antidepressants would you recommend?
A. Duloxetine
B. Fluoxetine
C. Paroxetine
D. Sertraline
E. Venlafaxine

Answer: B
The half-lives of the antidepressants are listed in descending order: fluoxetine (1–3 days), sertraline (26 hours), paroxetine (24 hours), duloxetine (12 hours) and venlafaxine (10 hours).
likely cause for her symptoms. Your answer is:
A. Acute confusional state
B. Generalised anxiety disorder
C. Hyponatraemia
D. Serotonin syndrome
E. Somatisation disorder

Answer: C
Hyponatraemia is common in old people receiving SSRI treatment. They present with lethargy, muscle ache and nausea. More severe cases present with cardiac failure, confusion and seizure.

9. Which of the following is least likely to be found in patients taking lithium when the lithium level is within therapeutic range?
A. Changes in ECG
B. Endocrine abnormalities
C. Nystagmus
D. Peripheral oedema
E. Weight gain

Answer: C
Nystagmus occurs in lithium toxicity.

10. A 50-year-old woman with bipolar disorder is admitted to the medical ward and the medical consultant discovers that she has thrombocytopenia. The consultant wants to find out which of the following psychotropic medications is most likely to be responsible for thrombocytopenia. Your answer is:
A. Lithium
B. Olanzapine
C. Quetiapine
D. Sodium valproate
E. Zopiclone

Answer D.
Sodium valproate is associated with thrombocytopenia although it is an uncommon side effect.

11. A 30-year-old woman suffers from bipolar disorder and she is very concerned that she became pregnant although she takes oral contraceptive pills. Which of the following medications have led to the contraceptive failure?
A. Lithium
B. Lamotrigine
C. Carbamazepine
D. Valproate
E. Topiramate

Answer: C
Carbamazepine is an inducer of cytochrome P450 and it has led to the contraceptive failure in this woman.

Revision MEQs

**A 70-year-old man is brought by his wife to the Accident and Emergency Department because he wanted to jump from his HDB flat. He has history of prostate cancer and the oncologist has started a new chemotherapy which results in side effects. He is concerned with somatic complaints and appears to be anxious during the interview. He has history of depression 10 years ago. His GP started fluoxetine 20mg OM two weeks ago but his symptoms have not improved.**

1. **Is his suicide risk high or low?**
This man has high suicide risk.

2. **List the tell-tale signs in the history which support your risk assessment.**
   1. Dangerous methods of suicide attempt – i.e. jumping.
   2. Old age, male gender.
   3. History of depression.
   4. Neurotic depression and preoccupation with somatic complaints.

3. **His wife is ambivalent about admission to psychiatric ward. State 4 reasons why this man should be admitted.**
   1. Prevention of suicide attempt.
   2. To find a right antidepressant or to adjust the dose of current antidepressant.
   3. To liaise with the oncologist about the side effects of chemotherapy.
   4. Refer him to see a psychologist for psychotherapy.

4. **If this man is admitted to the ward, what would you suggest the nurses to do?**
   To put this man under closing monitoring for suicide attempts [i.e. suicide precaution].

5. **He is concerned side effects of fluoxetine. Please list 5 common side effects associated with fluoxetine.**
   1. Anxiety
   2. Insomnia
   3. Nausea
   4. Headache
   5. Diarrhoea

References:


NICE guidelines on depression in adults


