В. В. Глущенко, Н. Н. Ильяшенко

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SYNDROME OF PSYCHOPATHOLOGY AND MENTAL DISEASES

Учебное пособие

Великий Новгород
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МИНИСТЕРСТВО НАУКИ И ВЫСШЕГО ОБРАЗОВАНИЯ
РОССИЙСКОЙ ФЕДЕРАЦИИ
ФЕДЕРАЛЬНОЕ ГОСУДАРСТВЕННОЕ БЮДЖЕТНОЕ
ОБРАЗОВАТЕЛЬНОЕ УЧРЕЖДЕНИЕ ВЫСШЕГО ОБРАЗОВАНИЯ
«НОВГОРОДСКИЙ ГОСУДАРСТВЕННЫЙ УНИВЕРСИТЕТ ИМЕНИ
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В пособии представлены современные подходы к оценке психики больного человека. Дана информация о психопатологических нарушениях, их номенклатура в соответствии с требованиями Международной классификации болезней 10 (МКБ-10). Описаны методические подходы к клинико-психопатологической диагностике и тактике медицинской реабилитации.

Предназначено для англоговорящих студентов и ординаторов медицинских вузов.

The training manual presents contemporary approaches to a patient'smental health assessment. It provides the information about psychopathological disorders, their nomenclature in accordance with the requirements of the International Classification of Diseases 10 (ICD-10). The manual offers a description of methodological approaches to clinical psychopathological diagnostics and medical rehabilitation strategies.

The training manual is intended for English-speaking students and resident physicians.

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ВВЕДЕНИЕ

Состояние психики человека имеет важное значение для возникновения заболеваний, особенностей их течения, прогноза, а также для повышения эффективности лечебных воздействий. Влияние врача, самовнушения больного могут существенно исказить картину болезни. Индивидуальный подход к больному обеспечивает как большую глубину и точность распознавания (диагностики) прогноза болезни, так и рациональный выбор наиболее эффективной терапии. Сказанное применимо к любому больному, независимо от характера его болезни.

Целью освоения учебного модуля является формирование прочных теоретических знаний и практических навыков в области психиатрии, необходимых для успешной профессиональной деятельности.

INTRODUCTION

Mental state is very important factor for the occurrence of diseases, peculiarities of its progression, prognosis, as well as for increase of effectiveness of therapeutic intervention. Influence of a medical practitioner, autosuggestion of the patient can significantly distort the aspect of the disease. An individual approach to the patient provides both better understanding and accuracy of recognition (diagnosis) of the disease prognosis, as well as a rational choice of the most effective therapy. The above said is applicable to any patient, regardless of the nature of his disease.

The goal of the training module is to develop solid theoretical knowledge and practical skills in the field of Psychiatry that are necessary for successful professional activity.

The purpose of this section is to introduce the reader to concepts that are relevant to understanding how symptoms of disturbed brain function present as mental symptoms. Psychopathology is the study of the symptoms of mental disorders and includes both the subjective account of the patient and descriptions of observed disturbances by the clinician. It involves the dissection and categorization of symptoms so that they can be understood in terms of clinical diagnosis and treatment.

1. What are the symptoms of disturbed brain function?

Disturbed functioning in the brain can produce a wide range of neurological and psychological symptoms and signs. Psychiatrists are especially interested in eliciting psychological (or mental) symptoms and understanding how they relate to psychiatric illnesses. These can include disturbances to behaviour, speech and language, mood and affective expression, thinking, perception and cognition. In addition, the ability to organize and sequence behaviour and integrate information to respond coherently can be affected by mental disorders. From a practical perspective, an important aspect of serious mental illnesses is that the ability to make rational decisions can be impaired in a way that sometimes require that patients receive help against their will, the so-called involuntary treatment, and which reflects a unique aspect of psychiatric care.

What is meant by the terms 'functional' and 'organic' when applied to mental disorders?

Historically, one of the ways of categorizing mental disorders has been to describe them as 'organic', wherein a reliable and discernible physical insult is identified as causing the disorder versus 'functional', wherein a consistent neuropathophysiological abnormality is not evident. It is important to recognize that this does not mean that symptoms of 'functional' mental disorder are any less 'real' but rather that the neural underpinnings are subtle such that they have not yet been identified in a way that allows for diagnosis by medical science. The biological era that has dominated psychiatry practice over the recent past was expected to unearth the underlying pathophysiology of common functional mental disorders. Although there have been considerable advances in understanding these conditions, disturbances that might allow for reliable diagnostic testing have remained elusive. In practical terms, all presentations of mental disturbances have a potential organic basis that should be ruled out before identifying them as functional. This is important when formulating a differential diagnosis, which should include possible physical causes and functional psychiatric conditions.

What is the difference between 'neurotic' and 'psychotic' symptoms?

Symptoms of mental illness can be divided according to their relationship to normal everyday experience. In psychosis, the person experiences symptoms that are outside the realm of normal experience and impact upon their experience of reality. These symptoms include delusions (abnormal beliefs that are not justified or rational) and hallucinations (perceptual experiences that occur without an

external stimulus). It is more difficult for clinicians to empathize with psychotic symptoms as they are typically not based upon a rational interpretation of reality and are outside normal experience. In contrast, neurotic symptoms include a variety of symptoms that are within normal experience but are excessive. Reality testing and insight are retained. These include anxiety, obsessive–compulsive phenomena and fears about health and wellness. The excessive nature of these experiences is a subjective judgement but closely relates to their functional impact. For example, many people experience intrusive obsessional thoughts that can be associated with compulsive behaviours (e.g. rechecking that the doors are locked and that appliances are unplugged at night). However, when this occurs at an intensity that interferes with one's ability to get to bed at a timely hour, it is considered pathological. Similarly, it is not uncommon to feel anxious in novel social circumstances, but when this anxiety is of an intensity that causes social avoidance that impacts upon one's quality of life, then it can be considered to have a pathological functional impact. The term 'neurotic' is also used, often in an uncomplimentary or pejorative way in everyday language (e.g. he or she is 'so neurotic') and has, thus, been largely retired. Nevertheless, the distinction between neurotic and psychotic symptoms is an important aspect of understanding psychiatric symptoms and diagnoses. In general, illnesses that include psychotic symptoms are more serious and are placed higher on the diagnostic hierarchy.

Do psychotic symptoms differ according to diagnosis?

Psychotic symptoms share the characteristic of being outside normal experience and linked to diminished insight on the part of the person experiencing the symptoms. Beyond that, they have quite different qualities or 'flavours' that allow them to be distinguished as organic versus functional, and affective versus schizophreniform. In organic psychosis, symptoms are typically quite simple and often relate to the immediate environment. Delusional ideas frequently include themes of paranoia about having things stolen or being poisoned or that their environment is not how it is represented, for example, medications are poisons being used to punish or harm and that the ward is a prison. Hallucinations are often in tactile or visual sensory domains, which are less common in functional psychosis where auditory hallucinations are the most common. Simple auditory hallucinations do occur in organic psychosis (e.g. noises in the background), but second- and third-person 'voices' expressing complex ideas are much more suggestive of functional illness. Delusional ideas in functional psychosis can often include complex and systematized patterns with bizarre or scientifically implausible content. Psychotic symptoms also have a different character in

affective versus schizophreniform presentations. At the core of understanding, this distinction should be made by considering the relationship of the experiences to prevailing mood state, and whether they are mood-congruent (which suggests an affective origin for psychosis) or not. Mood congruence reflects the extent to which the symptoms are in-keeping with or secondary to mood. In psychotic depressive states, delusional ideas typically have themes or nihilism, guilt or imminent death/serious illness and thus reflect a sense of self-reproach and hopelessness or pointlessness. In mania, delusional ideas are typically about empowerment, special abilities or talents, status, fame or wealth and thus reflect the elevation of mood with expansive and unduly positive thinking.

Other psychotic symptoms are not readily linked to mood as they are dominated by themes of persecution or passivity. In psychosis associated with schizophrenia and related disorders (e.g. schizoaffective disorder, delusional disorder), there is often an underlying theme of passivity, i.e. that an external force can influence or control aspects of one's experience that would normally be under one's own control (e.g. thinking, emotions, behaviour). The sufferer is unable to prevent this happening as it is outside their volition and is thus described using the phrase *passivity* . These symptoms are often referred to a 'schizophreniform' and include a variety of experiences that were first described by Kurt Schneider (1959) as symptoms of first-rank that are suggestive of schizophrenia and thus sometimes also referred to as Schneiderian first-rank symptoms. These symptoms include the external influence of thinking (inserting, removing or broadcasting thoughts) and third-person auditory hallucinations where the subject is commented upon or referred to in the third-person (e.g. 'he's trying to fool them that everything is all right') rather than directly addressed as in second person hallucinations (e.g. 'you are evil, you should harm yourself').

True versus 'pseudo' psychosis

Another distinction is between true psychosis and related symptoms that lack the quality of psychosis in terms of their perceptual nature and associated insight. This refers particularly to hallucinations where a true auditory hallucination is perceived like a true perception, i.e. in external space and as real. In contrast, auditory pseudohallucinations are often described as 'voices inside my head' that the person recognizes is not based upon a real external stimulus. Such experiences are often described as being distinguishable from normal experiences by their character (e.g. described as not sounding like a real voice). True hallucinations are perceived as having an external source. Similarly, for thought content, patients can present with abnormal ideas that are similar to delusions but

not held with the same intensity, are fleeting and relate to situational factors rather than an internal morbid experience. It is important to recognize that pseudo-psychotic symptoms are not 'false' or unimportant and that, in addition to occurring in vulnerable persons (e.g. emotionally unstable personality or those with dissociative disorder) and/or during periods of marked stress, they also commonly occur in major functional psychotic conditions, such as schizophrenia. These phenomena emphasize the importance of assessing serious mental symptoms in detail that should include their character, how they are experienced, their emotional significance, how they relate to events in the person's life and the conviction with which they are held (e.g. are they acted upon by the person?).

Neurosis and nonpsychotic symptoms

Traditionally, nonpsychotic symptoms of mental illness have been referred to as 'neurotic'. However, this term has been subsumed into the language of everyday life, often with a negative attribution ('you are so neurotic') that it has been largely retired by the psychiatry community. Nevertheless, the concept has some merit as it encapsulates mental disturbances that are often part of the normal experience of everyday life but that are exaggerated or experienced in excessive ways and therefore have a functional impact upon the person. In addition, the person recognizes that they are abnormal and has insight into their nature as evidence of mental distress or illness. Included among these symptoms are intrusive worries and ruminations, obsessional thoughts, compulsive behaviours, intrusive recollections of negative events, somatization and hypochondriacal. Central to this is that these are experiences that we all can recognize and often empathize with (e.g. experiencing stomach cramps when under stress or avoiding walking under a ladder on the street for fear it may bring bad luck). However, with illness, these symptoms become problematic in terms of impaired functioning (e.g. being late for work because of repeatedly checking that all the doors are locked and that appliances are unplugged).

Distinguishing between symptoms that relate to illness versus underlying personality

An important concept in understanding mental symptoms is how they relate to a person's underlying personality and belief systems. We all have beliefs that are shaped by our life experiences, cultural and religious background; that somebody with a different background may perceive as unusual or even abnormal. These ideas are not irrational but can be perceived as outside of normal belief systems for many other humans and are referred to as overvalued ideas. The ego can be understood as that part of the mind that mediates between the conscious and

unconscious. It is responsible for reality testing and gives a sense of personal identity. Overvalued ideas are typically 'ego-syntonic' in that they are consistent with our personal belief system and perceived as our own thoughts. In contrast, ego-dystonic thoughts are not consistent with our belief system and perceived by us as abnormal. Having thoughts about the need for cleanliness or order is a frequent ego-syntonic experience, but where these dominate thinking and cause anxiety if resisted, they become abnormal and are perceived by the person as undesirable and ego-dystonic. Obsessionality is a common (and often useful) personality trait, but having intrusive obsessional thoughts that lead to time-consuming and functionally disabling (compulsive) behaviours that are unwanted by the person are typically attributed to illness rather than a personality trait (e.g. obsessive–compulsive disorder [OCD]). Similarly, experiencing intrusive thoughts regarding behaviours, such as gambling or substance use, are typically viewed as ego-syntonic and not attributed to illness (although this distinction is increasingly challenged).Another important consideration regarding the nature of mental symptoms is their pattern over time. Personality is a relatively consistent phenomenon that is expressed in traits that are evident across the various domains of our life and that are stable over time. In contrast, most mental illnesses follow a phasic pattern over time with recovery (or relative recovery) between episodes. There is thus a distinction between difficulties that reflect a state or phase than those that persist as traits (i.e. state versus trait). This distinction is complicated by the fact that personality and illness are not mutually exclusive concepts such that persons with obsessional personality are more prone to developing obsessional symptoms when unwell (e.g. as part of depressive illness or OCD). Moreover, in many cases, psychiatric illness can involve persistent residual symptoms that over time share many characteristics of personality traits.

2. Disturbances to thinking

These can include abnormal content of thoughts or disturbed thought processes (i.e. the construction or mechanics of thinking). It is important to note that our ability to recognize disturbances of thinking is heavily dependent upon speech as this is the principal mechanism by which our thought processes and their content are expressed. As an example, patients with mania frequently present in a highly energized state that includes loud and fast speech with content that can rapidly switch from topic to topic. These phenomena are referred to as 'pressure of speech' and 'flight of ideas', which are considered disturbances of speech and thought-form, respectively. In such cases, patients can often express a variety of grandiose beliefs (e.g. having special abilities or being on an important mission) that reflect delusions, which are disturbances of thought content. Distinguishing between speech, language, thought-form and content could be challenging, and it is not necessary for students to necessarily distinguish the precise focus of the disturbance, but rather note its presence and significance.

Thought content. Disturbances to the content of one's thoughts is a fundamental component of most mental disorders. These disturbances range from thoughts that we all experience daily, and that are associated with psychic discomfort (e.g. anxious ruminations) to thoughts that are grossly bizarre and scientifically implausible (e.g. delusional ideas that one can control the weather through our behaviour). Some disturbances relate very directly to external experiences and specific life events (e.g. intrusive recollections with posttraumatic stress disorder [PTSD]), while others arise as part of an intense internal morbid experience (delusional ideas with emerging schizophrenia). It is thus important to explore abnormal thought content in terms of its principal theme, the impact upon the person's sense of well-being (safety, mental integrity) and emotional state, the plausibility of the beliefs, their relationship to past experiences, the capacity to resist or exclude the thoughts from one's mind, the conviction with which they are held, any associated actions and the willingness of the person to see the thoughts as reflecting illness.

Ruminations are any recurring thoughts or worries. Ruminating is repetitively going over a thought or a problem without managing to resolve the issue. It is commonly seen in depressive and anxiety disorders but is also part of the normal everyday experience where ruminating is part of the worrying or brooding process.

Obsessions are recurrent, intrusive, unwanted ego-dystonic thoughts, images or urges that are not inherently pleasurable. They are distressing and anxiogenic

and are often accompanied by a sense of compulsion. Attempts to resist obsessional thoughts are often associated with worsening anxiety. Themes include hygiene, contamination, safety, symmetry or order, and sometimes religious or bizarre sexual or aggressive themes. Some patients experience a sense of more general ' *obsessional angst* ' where they obsess about the meaning of things (e.g. life) or experience persistent thoughts about 'what if'. Obsessions are frequently associated with compulsive behaviours (' *compulsions* ', e.g. hand washing, checking) that are repetitive, and although goal-directed, they are ultimately without a useful purpose. Obsessional thoughts are common in all humans and often involve an element of magical thinking (e.g. 'if I count to ten repeatedly then my football team will score'), but with OCD, they are recognized as excessive and harm one's functioning.

Intrusive recollections are a specific type of recurring thought that is a feature of PTSD and refer to the person reliving a traumatic event through recurrent and intrusive thoughts or memories about the traumatic event. They are frequently accompanied by distressing nightmares or perceptual experiences, such as flashbacks (or 'daymares') with autonomic arousal. They are frequently triggered by situations that are of emotional significance or have symbolic relevance to the traumatic event (e.g. encountering violence on a television programme that reminds one of an assault).

Overvalued ideas are thoughts that are considered unusual or unreasonable by their intensity or conviction. They are strongly held but not to delusional intensity, in that the person typically has good insight into the fact that they are very personal and that others might not share them or may perceive them as unusual. They are usually understandable in the context of the individual's personality, culture or life experiences. An important distinction from overt psychosis (i.e. delusional ideas) is that insight is maintained as the idea is not unshakeable. Overvalued ideas may be featured in conditions, such as morbid jealousy, hypochondriasis, dysmorphophobia (a belief that one is abnormal in appearance) and anorexia nervosa. Political or religious extremism is sometimes explained in terms of overvalued ideas. In morbid jealousy, the person has an unjustified belief and excessive concern that their significant other is being unfaithful. This occurs most commonly as an overvalued idea (based upon a vulnerability in terms of personality, alcohol use issues or sexual dysfunction), but on occasions, can reach delusional intensity (so-called 'delusional jealousy'); in such cases, it poses a major risk for being acted upon with violence (including homicide). In such cases, it is important to carefully assess the nature of the beliefs and the extent to which they may be acted upon (e.g. checking personal

possessions, movements, phone activity). Of note, infidelity is not an uncommon feature of everyday life such that a key consideration is to what extent the person has justification for their suspicions. In morbid jealousy, the focus is typically more ego-centric and relates to the perceived betrayal by another person, while with infidelity, the focus is often upon how and with whom it is occurring. In short, where such beliefs occur as part of the illness, they principally relate to an internal morbid process rather than actual external evidence. Morbid jealousy is also sometimes referred to as 'Othello syndrome', referring to the character in Shakespeare's play, *Othello*, who murdered his wife as a result of a false belief that she had been unfaithful.

Delusions are often described as fixed, false beliefs that are not understandable in the context of a person's personality or background. They are not reasonable, often illogical and insight is lacking. Classically, fully formed delusions are all of the above, but it should be noted that in the emerging stages (or as the ideas soften as one recovers) delusional ideas may not be held with absolute certainty. In addition, delusions are not necessarily false–the partner of a person who has delusional jealousy might also be unfaithful! Moreover, delusional themes are frequently shaped by one's personality or background and are therefore not entirely independent of these. In the 20th century, religious themes were extremely common in delusions, while in the 21st-century, themes that relate to technology and the internet are very common.

Delusions can involve a variety of different themes that can assist with diagnosis (see table 1). Delusions can be classified in terms of whether they are bizarre or non-bizarre (often in terms of whether they have any plausibility). Bizarre delusions are implausible, are not derived from normal life experience and are difficult to understand. For example, a patient may feel that aliens are transmitting messages to the chosen people through a radio transmitter implanted in their brain. A good example of a non-bizarre delusion would be delusions of love or infidelity; while they may be false, they are not beyond the realms of possibility. Bizarre delusions are more indicative of a schizophrenia-spectrum disorder. Delusions could also be primary or secondary. Primary delusions (also called 'autochthonous delusions') cannot be understood because of circumstances or events or are secondary to one's mood state. Conversely, secondary delusions relate to the prevailing mood (grandiose delusions in mania or delusions of guilt in depression) and can also occur as secondary to a primary delusion (e.g. 'I can save people from damnation' may be secondary to a primary delusion that 'I am God's special messenger').

Table 1. Delusional Themes

Delusional Theme	**Example**
Delusions of reference	The belief that others are paying undue attention to one by monitoring one's behaviour or communicating abnormal ideas through the television, radio, internet or other means.
Delusionsof control/passivity	The belief that an external agent is interfering with one's thoughts, actions or emotions.
Delusions of persecution	The belief that other(s) are attempting to cause one harm or are interfering with one's privacy, reputation or ability to prosper.
Delusions of grandiosity	The belief that one has special abilities, attractiveness, wealth or status.
Delusions of guilt	The belief that one is responsible for bad events or has committed a terrible action.
Delusions of jealousy	The unjustified belief that one's partner is unfaithful.
Hypochondriacal delusions	Delusional belief that one has a specific illness.
Nihilistic delusions (Cotard's syndrome)	The belief that one does not exist, is already dead or putrefying, or that they have lost their blood or body parts/organs.
Delusional Misidentification Syndromes	
Capgras syndrome	The belief that a spouse or close relative has been replaced by an imposter.
Fregoli delusion	The delusion of doubles where there is a belief that a person, often a stranger, is a familiar person in disguise. Typically the delusional person believes that they are being persecuted by the person they believe is in disguise.
Intermetamorphosis	The belief that people can swap identities with each other but appear the same.

The experience of a primary delusion can have different elements or follow recognized themes that are: (i) delusional mood, which is the vague feeling that 'something is not quite right', but that the nature of what is different is not yet clear; (ii) delusional intuition, which involves the occurrence of sudden, out-of-the-blue delusional ideas; (iii) delusional perception, wherein a normal object or perception is attributed a delusional meaning (e.g. a traffic light changed from green to red, and the person realized that he had been chosen to lead people into the promised land); and (iv) delusional memory, wherein a person remembers an event but belatedly attributes a delusional significance to it. The concept of primary delusions is often debated by psychiatrists. However, ultimately, if a

patient experiences delusional ideas without any plausible basis or understandability in terms of other mental phenomena, then they can be considered primary and raise the possibility of a diagnosis of schizophrenia or related conditions.Some themes for delusional ideas are described in table 1.

Delusions of thought interference/control. One type of delusion that has importance is that in which the person believes that their thoughts are being interfered with by an external force. At the core of these experiences is the sense of a loss of integrity or control over one's thoughts (and therefore, private space and autonomy), which is referred to as 'passivity'. Three main patterns occur: thought withdrawal, thought insertion and thought broadcast. In thought insertion, thoughts are ascribed to other people who intrude their thoughts. Patients often report that these thoughts have been 'put there by others' and do not recognize these thoughts as their own. In thought withdrawal, the person describes a sense (often as a sensation of feeling the thoughts being extracted) of their personal thoughts being removed by an external force and against their will 'my thoughts are being taken from me by others'. This is different from thought blocking where the person experiences a sense of being unable to generate thoughts and feeling mentally blank rather than that their thoughts being actively removed. Thought broadcast is the belief that one's private thoughts are accessible to others without having revealed them (i.e. that their internal thoughts are being broadcast to others who can therefore know what the patient is thinking). Patients will typically complain that 'others can read my mind'. Eliciting these phenomena may seem daunting to the novice interviewer and patients who have not had these experiences may find the questioning strange or even upsetting. However, these phenomena can be gently probed for using the usual pattern of beginning with relatively open questions (e.g. 'do you ever feel that people are trying to influence your thoughts or feelings?' and 'have you ever experienced telepathy?'), subsequently proceeding to more specific questions, such as 'have you ever had the experience of feeling that the television or radio (or internet) is referring to you in particular or trying to influence your thoughts?'; 'have you ever felt that some of your thoughts are not your own or have been placed there by others?' or 'do you ever feel that people can read your mind?' Delusions of thought interference are important phenomena as they are highly suggestive of schizophrenia and related conditions.

Thought-form. Disturbances to thought processes are often referred to as formal thought disorder. They involve a spectrum from excessively concrete thinking ('if it's raining cats and dogs, why cannot I see any animals' or 'I cannot explain what you mean by "a stitch in time saves nine" because I have no interest in embroidery') to thinking that is unusually loose with regard to the connection between thoughts, thus creating difficulties to converse coherently and

understandably (so-called ‘loosened associations’). A description of the more important abnormalities of thought-form is presented in table 2.

Table 2. Examples of Types of Thought Disorder

Flight of ideas/clanging	Abrupt changes from topic to topic but with discernible links between topics. This is frequently accompanied by ‘clanging’ whereby successive thoughts are linked by rhyming rather than meaning, e.g. ‘Dr Marr, will go far, in his superfast car, ah ha ha’ (classically associated with manic states).
Loosening of associations	The connection between thoughts is loosened and contains only remotely related ideas. The frame of reference of thoughts changing from sentence to sentence such that there is a rapid shifting from topic to topic without highly obvious connections. In a mild form, this can be considered as lateral thinking and underpins much good art (e.g. poetry). However, in psychosis, it can significantly impair the ability to conduct a coherent conversation in which case it is often referred to as ‘tangentiality’. ‘Knight’s move’ thinking refers to the nonlinear direction of thoughts that seem to move in two directions at once like the knight on a chessboard. ‘Derailment’ occurs where the person loses their train of thought and does not return to the original point.
Poverty of thought/thought retardation	Thinking is slowed with fewer thoughts entering consciousness (classically associated with depression).
Thought block	Abrupt interruption to train of thought whereby the person feels that their thoughts suddenly stop and they ‘draw a blank’ (seen in psychotic conditions (especially schizophrenia) but also common in the general population at times of fatigue or stress (e.g. drawing a blank in an exam).
Perseveration	Persistent repetition of words or ideas beyond the point at which they are relevant (most frequently seen in organic illness and classically linked with frontal lobe pathology).
Circumstantiality	This is similar (but milder) to tangentiality whereby the pattern of thinking follows a nonlinear route with drifting focus but that eventually comes back to the point. Nonessential and irrelevant detail causing a delay in getting to the point (can occur in psychosis, temporal lobe epilepsy or as a manifestation of obsessional personality).
Incoherence	Thinking and its expression through speech becomes so lacking in structure as to be incomprehensible. The person voices actual words, but these do not allow for a coherent sentence and can result in what is essentially incoherent gibberish, referred to as ‘word salad’ or ‘jargon aphasia’ (seen in schizophrenia, severe mania and organic states, such as progressed dementia).

3. Abnormalities of perception

Abnormalities of perception can occur in any of the five senses–visual, auditory, gustatory, olfactory or tactile. The nature of any disturbances is defined by their relationship to external stimuli and the personal appreciation of their significance. In general, a perceptual experience may be a sensory distortion or deception. Sensory deceptions are further divided into illusions and hallucinations.

Sensory distortions. These occur when real objects are perceived as altered in some way–either in terms of their physical character (quantitative) or significance (qualitative). Qualitative distortions are frequently associated with drug toxicity and affect visual perception; for example, the colour of an object may seem altered. With quantitative alterations of perception, the size or shape may be altered. Micropsia occurs when an object is perceived as smaller than reality; macropsia occurs when an object is perceived as larger than reality; and dysmegalopsia occurs when the object appears altered in shape. These are associated with organic diseases, such as epilepsy, drug intoxication and withdrawal states. The main types of sensory distortion are listed in table 3.

Table 3. Sensory Distortion

Description	Diagnostic Significance
Changes in intensity (hyperaesthesia or hypoaesthesia)	
Increased sensitivity to sound (hyperacusis)	Anxiety, depression, migraine, alcohol withdrawal, autistic spectrum disorder, fatigue
Reduced to sound sensitivity (hyporacusis)	Delirium, depression, ADHD
Intensification of colour	Hypomania, LSD intoxication, intense normal emotion, e.g. romantic or religious experience
Reduced intensity of colour	Depression (everything is grey or black)
Reduced gustatory sensation	Depression (all food tastes the same)
Changes in quality	
Altered colour of the image (yellow, xanthopsia; green, chloropsia; red, erythropsia)	Intoxication with a variety of substances, especially hallucinogens, such as LSD or psilocybin, and also digoxin toxicity
Objects appear unreal and strange (derealization)	Mood and anxiety disorders, TLE, migraine, drug intoxication and withdrawal, states, fatigue
Change in form/shape (dysmegalopsia, metamorphopsia)	Visual problems, aura, epilepsy, schizophrenia ADHD, attention deficit hyperactivity disorder; LSD, lysergic acid diethylamide; TLE, temporal lobe epilepsy.

Sensory deceptions. Sometimes called 'misperceptions' these involve a new perception that may (illusion) or may not (hallucination) be in response to external stimuli.

Illusions are false perceptions of an external stimulus that are frequently associated with prevailing affect and occur when stimuli from a perceived object are combined with a mental image to produce a false perception. They are not necessarily indicative of psychiatric pathology. Three types are described: completion illusions, affect illusions and pareidolia. Completion illusions are when an incomplete or incorrect object, for example, an incomplete drawing or incorrect spelling, is perceived as complete or correct. We have an innate impulse to make sense of our experiences and as such, use experience and knowledge to fill in the gaps. Consequently, we perceive a different object to what has been presented. An example would be to see CCOK and perceive COOK as it makes more immediate sense. Affect illusions occur when the person's emotional state leads to misperceptions; for example, being frightened walking along a dark road may lead to the incorrect interpretation of a shadow from a tree as something more threatening, e.g. muggers. Pareidolia is when an individual perceives a meaningful image in a random or ambiguous visual pattern (such as flames of a fire, or in clouds). Examples would be the Rorschach test–seeing the man in the moon or the face of Jesus in a bowl of cornflakes.

An hallucination refers to when perception occurs in the absence of a stimulus. Hallucinations are false perceptions. To the person, they seem to be occurring in external space ('without') even though they arise from 'within'. They are not under voluntary control and possess the substantiality of normal perception. They may be auditory, visual, olfactory, gustatory or somatic. Not all are of pathological significance. Auditory hallucinations are especially relevant to functional psychiatric conditions and have different characteristics according to the underlying diagnosis. Third-person hallucinations (e.g. where the person is referred to as he or she, discussed or commented on by voices) are suggestive of schizophrenia and related psychoses. Command hallucinations are important by their capacity to provoke behaviour, especially that which involves risk to self or others. The degree of compulsion to act upon command hallucinations must be clarified. From a functional perspective, hallucinations may be classified as functional, reflex, extracampine or autoscopic. Different categories of hallucinations are described in tables 4 and 5 , below.

Table 4. Types of Hallucination

Hallucination Type	Description	Diagnostic Significance
Third-person auditory hallucinations	The patient hears voices referring to him/herself in the third-person, e.g. 'he/she is a bad person'	
Thought echo/echo de la pensée/ Gedankenlautwerden	The patient hears his or her own thoughts aloud a short time after thinking them	Highly suggestive of schizophrenia
Running commentary	The voices consist of hearing a 'running commentary' on the patient behaviour, e.g. 'she is drinking tea'	
Second person auditory hallucinations	The voice addresses the patient in the second person, e.g. 'you are a bad person'	Occurs across a range of psychotic presentations, including affective schizophreniform and organic disorders
Visual hallucinations	Seeing an object that is not there, a false perception of vision	Suggestive of organic pathological conditions, such as delirium, dementia, tumour, hallucinogenic drugs
Olfactory hallucinations	False perception of smell	TLE, schizophrenia, depression
Gustatory hallucinations	False perception of taste	Schizophrenia, TLE
Somatichallucinations	Sensations, e.g. heat, cold, electricity, visceral sensations affecting the skin, muscles, joint sense or internal organs; 'tactile' hallucinations describe sensation affecting the skin, and 'haptic' refers to hallucinations of touch; formication is a sensation of animals/insects crawling under the skin	Schizophrenia, organic psychoses, cocaine intoxication (formication)
Elementary hallucinations	Unstructured hallucinations, e.g. whirring noises (auditory), multicoloured spots (visual)	Not necessarily indicative of psychiatric illness
Negative hallucinations	The absence of perception despite the presence of a stimulus	Not necessarily indicative of psychiatric illness
Pseudo-hallucinations	Experienced in the inner subjective space. Lack of reality of true perception TLE, temporal lobe epilepsy.	Not necessarily pathological

Table 5. Classification of Hallucinations

Hallucination	Explanation
Functional	Stimulus provokes the hallucination, and both are perceived in the same modality, e.g. hear the tap running and hear voices
Reflex	A stimulus in one modality provokes a hallucination in a different modality, e.g. seeing an angel when a bell rings; this may be a morbid form of synaesthesia, where one sees letters as colours
Extracampine	Hallucinations that are outside the normal field of the particular sense, e.g. seeing a person who is in a different country
Autoscopic	The experience of seeing oneself. The person 'remains' in their own body unlike with dissociative (or 'out of body') experiences where the person sees their own body from a vantage point outside their physical body; associated with migraine, epilepsy, organic psychoses and drug intoxication
Distinct formed	Elderly patients with normal consciousness and no brain pathology, but with reduced visual acuity due to ocular problems experience vivid, distinct formed hallucinations, often of men wearing hats. This is called Charles Bonnet syndrome
Lilliputian	Hallucinations involve seeing tiny people or animals. These can occur with alcohol withdrawal

Flashbacks. A flashback is a perceptual experience whereby the person has a sudden, usually powerful, re-experiencing of a past experience. They are sometimes referred to as 'daymares' or involuntary recurrent memories. Typically, flashbacks are triggered by psychologically symbolic experiences one encounters in the current time that stimulate intense recall of a previous event from memory. Flashbacks can involve a variety of emotions, including joy, sadness and fear and can occur as part of normal experience. However, in psychiatry, the term is predominantly used to describe perceptual disturbances of PTSD and related conditions where the person has re-experiencing phenomena relating to traumatic events. These can include intrusive recollections, nightmares and flashbacks that are associated with marked autonomic arousal. Flashbacks occur involuntarily. The person typically recognizes that the experience is not 'real' but it can be so intense that the person 'relives' the experience during which they may struggle to recognize it as memory and not something that is happening in real-time. As such, flashbacks can provoke marked distress and hyperarousal with actions to remove themselves from the triggering stimulus. Therefore, more severe flashbacks can appear very similar to hallucinations, although their situational character and close

relationship to previous traumatic experience usually allow for them to be distinguished from hallucinations.

Derealization and depersonalization. Perceptual disturbances can also occur with qualitative alterations in consciousness. *Dissociation* is a mental process whereby the person becomes disconnected to their sense of self, including thoughts and feelings, and sometimes, can include a sense of being outside of oneself and watching themselves from above like an actor in a play. This can occur in states of extreme stress or trauma and with substance-induced states. Ketamine is an analgesic anaesthetic agent that can have marked dissociative effects with the so-called 'out of body experiences'. *Derealization* (a sense that the world around is not real) and *depersonalization* (a sense of detachment or being outside oneself as though watching a movie where one feels detached from other people). Both are frequently associated with a sense of the speed of time being altered and a general sense of fogginess or being in a dream. Deja and Jamais Vu can also occur. Derealization and depersonalization can be part of normal experience (e.g. when fatigued) and occur at elevated frequency across a range of mental disorders (e.g. mood and anxiety disorders) and in organic brain disorders where they are classically linked to temporal lobe activity and are a well-recognized feature of temporal lobe seizures.

4. Abnormalities of mood and affect (emotion)

Abnormalities of mood are the most common symptoms encountered in psychiatry. Mood is defined as a prolonged emotional state and can be characterized both subjectively by the patient and objectively by the clinician. Affect is the expression of emotional state at a point in time and is inferred objectively. These concepts are sometimes likened to the relationship between weather and climate–mood refers to a sustained emotional 'climate', while affect refers to more fluctuating changes in the emotional 'weather'. Normal mood is referred to as euthymia or normothymia, while normal affect is often referred to as appropriate in expression and range (or resonance). A depressed mood is characterized by feelings of sadness often with a sense of hopelessness, despondency and/or apathy. An elated mood is characterized by a sense of happiness or cheerfulness. These emotional states are part of the everyday experience but become pathological when they are excessive or not justified by circumstances. In mania, for example, the sense of happiness is frequently unshakeable even in the face of adversity (such as hospitalization or negative life events). Elated patients may, for example, describe hospital food as 'superb!' Several other terms can be used to describe mood states, such as dysphoric, euphoric, dysthymic, hyperthymic and ecstatic. Dysphoria describes a negative mood state that reflects mental discomfort and unhappiness that is frequently used when a person is discontent for reasons that may not relate to a sustained lowering of mood as we would typically expect in depressive illness. Euphoria is a state of elated mood that implies an organic focus (e.g. frontal lobe lesions, end-stage dementia) where a sense of excessive well-being is expressed because of an apparent loss of emotional regulation. Ecstasy refers to a state of intense joy and contentment that relates to a religious experience or positive life events (victory in sports, success in examinations, childbirth). Furthermore, elation, euphoria and ecstasy all describe mood states that include happiness but differ in terms of their relationship to other factors, such as other aspects of psychopathology, the context in terms of life events and apparent cause. Dysthymia describes a state of persistent low mood that is less acute and less severe than depression that was previously considered as a 'depressive personality'. In recent times, dysthymic disorder has been viewed as closer to depressive illness than personality disorder in character. Similarly, hyperthymia relates to a sustained tendency towards exceptionally positive mood and disposition. Mood can sometimes be described as anxious or irritable if they are the dominant emotional states of the person. Mixed affective states occur where there are contrasting elements that occur together

simultaneously or over short periods. ‘Dysphoric mania’ is an example where there are features of mania and depression with restlessness, irritability, unhappiness and pessimism. Agitated depression is a similar concept where the person has depressed mood but with agitation rather than the classical psychomotor slowing that is associated with many depressive episodes. Disturbances of affect can be in terms of its appropriateness of expression (‘blunting’), stability (‘lability’) and resonance (‘flattening’). Blunt (or incongruous) affect is one that lacks sensitivity to or consistency with circumstances, for example laughing in response to receiving news of a death or accident to a close one. It is seen in chronic schizophrenia, schizoid personality and autistic spectrum disorder. Flat affect is where the range of affective expression has become reduced (or flattened) and is typical of depressive illness where the emotional state remains despondent even in the face of news that would usually be received positively and with joy (e.g. winning money or succeeding in an interview or examination). A labile mood is one that is prone to fluctuation. This is typical of manic states where an elated and jovial person can rapidly switch to marked irritability.

5. Abnormalities of consciousness

Consciousness can be thought of as awareness of experience and can be considered both quantitatively (arousal and alertness) and qualitatively (comprehension and awareness). Cognition refers to the mental processes involved in understanding and processing experience of the world around us. These include attention, orientation, memory, comprehension, visuospatial reasoning and problem-solving. From a quantitative perspective, consciousness level falls along a continuum that ranges from being hyperalert to having full alertness and awareness to reduced arousal with stupor (where the person is minimally responsive) and ultimately coma (where the person is unresponsive to external stimuli). The impairment of consciousness is an important feature of organic illness. In delirium, for example, consciousness can be affected both qualitatively ('clouding') and quantitatively in terms of arousal, with both reduced arousal and hyperaroused states possible. 'Clouding of consciousness' is a descriptor that is used to describe qualitative changes to consciousness that impede the grasp of the environment. The person is in a cloud or fog that separates them from the clarity of usual awareness. The term is largely interchangeable with 'confusion'. These terms equate with a combination of impaired attention and diminished awareness. The fluctuation of consciousness refers to a pattern of consciousness that changes over time, for example, in delirium. The patient may become more disorientated in the evening when they are tired, and when the anchors of the day are less evident (diurnal fluctuation of consciousness sometimes called 'sundowning').

Consciousness and symptom generation: hysteria, factitious disorder and malingering.

A further consideration is a relationship between conscious and unconscious factors in mental symptoms. Traditionally, the term 'hysteria' has been applied to symptoms where the person is not conscious of the origin of their symptoms which are deemed to occur unconsciously. Dissociative disorder, somatic symptom disorder and conversion disorder (CD) are examples of this phenomenon. CD relates to patients who present with neurological symptoms (e.g. blindness, seizures or fainting, weakness or paralysis, problems swallowing or dysphagia) which are not consistent with a well-established organic cause and relate to a psychological trigger, such as stress. CD has been relabelled as 'functional neurological symptom disorder' in the Diagnostic and Statistical Manual of Mental Disorders-5. The relationship between conscious and unconscious factors in such presentations is complex in that the level of visible distress of the person is

frequently much less than one might expect given the symptoms, suggesting that the person has an awareness that their loss of function is not necessarily based upon serious physical pathology. This disconnect is sometimes referred to as 'La belle indifference'. In simple terms, these presentations are thought to reflect the fact that the person is psychologically unable to deal with a stressor and thus expresses (or 'converts') their distress through often compelling physical symptoms. These presentations are less common in modern practice, perhaps reflecting a greater general psychological awareness in society and the destigmatization of mental illness. In-keeping with this possibility, they are more common in persons from lower socio economic groups, those who are less educated, from rural backgrounds and in developing countries. Of note, symptoms of hysteria should be distinguished from factitious disorder and malingering. While dissociation and conversion are unconscious and reflect an abnormal coping mechanism used, for example, to avoid a stressful or intolerable situation, factitious disorder and malingering are consciously mediated (i.e. the patient is purposely faking the symptoms). Factitious disorder and malingering differ in respect of motivations for the deception. In malingering, the reason for the deception is tangible and rationally understandable, such as evading criminal prosecution, obtaining financial compensation, avoiding work or military duty or as means of obtaining drugs. In factitious disorder, the motivation is a pathological need for the sick role. Moreover, factitious disorder is considered a mental illness, whereas malingering is not.

Abnormalities of speech and language. A patient's speech, language and ability to converse may give the examiner valuable clues as to their diagnosis. It is important to note that one's speech is the vehicle by which thoughts are communicated, and there is an overlap between abnormalities of speech and thinking. Formal thought disorder, for example, might be communicated through grossly disorganized speech that can at times be virtually incomprehensible and described as a 'word salad'. In addition, there are several abnormalities of speech production, organization and content that clinicians need to recognize. Disturbed speech production includes dysphonia, dysarthria and dysphasia (with aphonia, and aphasia reflecting a total rather than partial loss of function). In dysphonia, there is difficulty in vocalization (e.g. speaking with a whisper) which can reflect lesions of the vocal cord or as a hysterical phenomenon. Dysarthria relates to motor difficulties in speech production that can occur after cerebrovascular accidents or can relate to muscular difficulties in the mouth and larynx, for example, extrapyramidal effects of medication. In dysphasia, the difficulty is with understanding or producing words and is thus primarily a language rather than

speech disorder. Stuttering, also known as stammering, describes a disturbance in the flow of speech with repetitive jarring at certain words or syllables. It is frequently unrelated to mental disorder but also can occur as a manifestation of anxiety (especially in children) and in the aftermath of severe trauma later in life. The flow of speech is also frequently altered in mood disorders with fast and often loud 'pressure of speech' in hypomania and mania and slowing of speech, often with a soft-spoken voice in depressive states. The organization of speech is closely related to thought processes. It can vary from characterologically determined overinclusive speech that may involve circumstantiality (a failure to get to the point with efficiency), logorrhoea (excessive wordiness, often with considerable repetition) and tangentiality (where the conversation repeatedly veers off the principal subject with oblique or irrelevant content). Perseveration is the persistent repetition of words or ideas beyond the point at which they are relevant. These disturbances are often an expression of obsessional or schizotypal personality traits but are also more common in people with schizophrenia and those with organic brain disease. The content of speech is also impacted by mental disorders. In mania, there is often colourful or flamboyant content (sometimes with rhyming or musicality called 'clang associations') because of the expansive thinking that is typical of that state (e.g. 'Dr Marr, will go far, in his superfast car, ah ha ha'). In depressive illness and chronic schizophrenia, there can be a poverty of speech or even alogia or muteness. Psychotic disorders can also include unusual use of language with made-up words ('neologisms') or the use of recognized words but with a personalized meaning that is not usually attributed to them ('metonyms'). Neologisms (or 'new' 'words') can sometimes endure and then become part of the mainstream language (e.g. 'mansplaining' as a verb to describe a male talking down to a female in a patronizing way, or 'confubble', which means to confuse and befuddle). Neologisms are frequently cannibalized from two words which are spliced to create the new phrase. Metonyms are recognized words used in a way that communicates a new concept, e.g. 'Washington' when referring to the United States Government. Metonyms are frequently encountered in good poetry where they can bring lateral thinking to the content.

Cognition is the process by which various cognitive functions allow a person to appreciate and respond to the world around them. These cognitive functions relate to different neuropsychological domains (attention, orientation, comprehension, memory and executive function) that can be tested during the psychiatric assessment. This should be distinguished from the concept of 'cognitive set' which relates to how a person perceives themselves in their interactions with the surrounding world and is typically altered in depressive states

(so-called cognitive distortions that include an unduly negative self-perception). While the majority of mental disorders impact upon cognitive function in some way (e.g. attention and short-term recall, which are decreased in depressive states and the early phases of psychosis), in organic brain disorders cognitive disturbance is the primary or core feature (e.g. attention is particularly impaired in delirium, while impaired short-term memory is characteristic of dementia). In contrast, disturbances to mood, thinking and perception are considered as secondary aspects.

Attention is the focusing of consciousness on a stimulus. Therefore, consciousness is necessary for attention. Attention can be voluntary or involuntary, the former being associated with consciously focusing on an event and the latter when the event attracts the subject's attention (e.g., a car back-firing). Attention can be further subdivided into focused and sustained attention (sometimes called 'vigilance'), with the former relating to the ability to direct and focus attention over seconds, with the latter reflecting the ability to extend this attention to a task for sustained periods–typically more than 10 seconds and often extending to minutes and longer. This can be described as the 'attention span', which is typically between 10 and 20 minutes in teenagers and adults. The relevance of attention span to education was demonstrated in a classic experiment where it was found that the average duration that students could maintain attention from the start of a didactic lecture was 11 minutes! The ability to perform tasks that require sustained attention impacts various activities of daily life, such as watching a television programme to the conclusion, or reading an article in the newspaper in its entirety. Selective attention is a further aspect of attention that relates to the ability to direct our focus to relevant stimuli while ignoring irrelevant stimuli in the environment. This is a valuable ability as we have a limited capacity in terms of how much information can be processed at a given time, and selective attention allows us to focus on what is important while deprioritizing less significant elements.

Orientation is the ability to gauge time, place and person accurately. Orientation to time is generally disturbed first, followed by place and then the person. Disorientation to a person can relate to significant others (e.g. what does that person (key nurse) do for a living?) which is considerably more common than loss of orientation to self which usually relates to severe or highly progressed organic brain disease (the 'mirror sign') or hysterical 'fugue' states where the person loses conscious awareness of their previous identity. It is important to take a flexible stance in terms of the distinction between understandable inaccuracies in responses to questions regarding orientation, especially in elderly persons who have been in hospital for prolonged periods during which their normal daytime

pattern and weekly routine do not occur. As a general rule, it is rare for a normal individual to misidentify the year or the month, but as many as 5% of older patients may misidentify the date (day of the month), especially when they have been in hospital for more than a week. Orientation to place reflects the ability to communicate one's location (including its significance), such as that they are in a hospital or an outpatient clinic or at home and can extend to naming the town or city where that location is. Impaired temporal and sometimes spatial orientation can occur in states of intoxication or fatigue.

Torpor syndromes can have different depths, depending on which the following terms are used : "obnubilation" – clouding, derangement of consciousness, cloudiness of consciousness; "somnolence" which is sleepiness; further, we have "sopor" – unconsciousness, insensitivity, pathological sleeping; the final stage in this round of syndromes is "coma" – the deepest degree of cerebral insufficiency.

6. Disorders of Memory

Memory is a highly complex component of cognition that can be considered from a variety of perspectives, including temporal aspects and content. In crude terms, memory can be tested for registration, short-term recall and ability to remember events from the immediate past (intermediate memory) and distant past (long-term memory). Memory can also be autobiographical (relating to personal events and experiences) or procedural (relating to skills or knowledge of procedures sometimes called memory for 'how to'). Declarative memory can be divided into episodic and semantic memory. Episodic memory is for experiences and specific events in time in a serial form, including autobiographical events (times, places, associated emotions and other contextual knowledge) that can be explicitly stated or 'declared'. Of note, the context and associated emotions are included in this part of memory. Semantic memory is a more structured record of facts, meanings and knowledge about the external world that are acquired over time. It refers to general factual knowledge that is abstract, relational and independent of personal experience and of the context in which it was acquired. It includes things, such as vocabulary, capital cities, social customs, understanding of mathematics and functions of objects. Procedural memory relates to the store of knowledge that relates to being able to perform tasks. It is implicit and less readily stated or declared. Knowing how to drive a car, ride a bicycle or swim are examples of functions that exercise procedural memory. It typically operates at an unconscious and automatic level and without awareness of the previous experiences that shaped the memory. The principal aspects of memory that are relevant to the practising clinician are impairments of short-term memory, which occur in patients with dementia, post-seizures (including after ECT) and in those with traumatic brain injuries, and a variety of presentations that include expression of memories that are not accurate. Disorders of memory can be divided into amnesia (where there is a loss of the content of memory) and paramnesia (where the content of memory is distorted or inaccurate). Some examples of clinical phenomena that reflect these types of memory disturbance are presented in table 6. Anterograde amnesia describes the failure to create new memory from a particular point (e.g. a head injury with loss of consciousness) and retrograde amnesia where memory for incidents prior to an event are lost. This is typically of the period immediately preceding the event but also sometimes of longer-term, stored autobiographical memory. Impaired registration with reduced short-term memory can occur in any mental disorder where registration is impeded by poor attention and distractibility (e.g. major depression, anxiety states, ADHD and delirium).

Table 6. Disorders of Memory

Memory Disturbance	Description
Amnesia	
Psychogenic/hysterical/dissociative amnesia	Sudden retrograde episodic memory loss with amnesia for personal identity and personal events. Might be associated with a fugue state where the person travels away from their usual place in which they operate and may be found wandering and lost. Social skills and personality are maintained. It is said to occur in the context of extreme trauma and is usually short-lived (hours to days).
Blackouts	Discrete periods of anterograde amnesia particularly associated with alcohol intoxication.
Paramnesia	
Retrospective falsification	Deliberate or unconscious alteration of memory for past events or situations used as a mental mechanism for ego preservation and reflecting the current emotional, experiential and cognitive state. For example, in depression, a patient may describe all their past failures while ignoring their achievements.
False memory	A person will recall events that they strongly believe took place but did not take place.
Screen memory	A memory which is partially true and partially false. This is thought to occur when the entirety of the true memory is too painful.
Confabulation/falsification of memory	In confabulation, the patient may fabricate, distort or misinterpret memories without the conscious intention to deceive, rather, the patient is filling in gaps in memory with imagined or untrue experiences. It is associated with organic brain disease and classically with Korsakoff's syndrome.
Pseudologia fantastica/ pathological lying	This term describes confabulation in the absence of organic brain disease. The individual may describe major traumas or grandiose ideas. Munchausen's syndrome is a variant where the subject feigns illness or psychological trauma to gain sympathy or attention.

Visuospatial function refers to that aspect of brain function that identifies and integrates visual phenomena, such as shape, depth and spatial relations. It is the cognitive function that underpins understanding and navigating our

environment and the structures contained therein. In clinical settings, it can be assessed through the ability of the patient to reproduce a visual image, including its component elements. Conventionally, this is assessed through drawing tests (e.g. the clock drawing test, the interlocking pentagons test), the ability to perform functional tasks, such as dressing, making a bed, assembling items and the patient finding their way around the environment. Disturbances to visuospatial abilities occur in the context of general cognitive impairment, but they are also disproportionately affected in delirium and in conditions that include lesions of the occipito-parietal cortex.

Executive functions are those aspects of brain function that underpin organization and planning, concept formation and word/idea generation. They involve several processes, such as working memory, cognitive flexibility, inhibitory control and other complex functions as planning, problem-solving and abstract reasoning. Deficits of the executive functions are observed in all populations to varying degrees, but more severe executive dysfunction occurs in organic brain syndromes, functional psychotic illnesses, ADHD and autism. These cognitive deficits affect routine functioning in personal, social and vocational activities, as well as worsen the clinical course of the disease by impacting upon treatment adherence. A scheme for assessing cognitive function while at the bedside is described in Box II.6, above.

Insight. Insight is a key concept in psychiatry that distinguishes many more serious mental illnesses from the rest of medicine, and that underpins the need to consider treatment that is without the person's consent. In this respect, psychiatry significantly differs from medico-surgical care, where most patients present actively seeking help. In contrast, approximately one in ten admissions for psychiatric care occur using procedures defined in law for involuntary treatment. In addition, insight is a key factor that impacts upon adherence to treatment plans. It is important to recognize that insight is not a static, fixed concept and can change as the patient's mental health improves or worsens. The following questions are useful in assessing insight:

1. Does the patient recognize their current 'problems' as symptoms of being unwell or experiencing illness?
2. Does the patient believe that the illness is a psychological/mental illness?
3. Does the patient recognize the need for treatment?
4. Is the patient willing to accept treatment?

Insight is thus a multidimensional construct that includes the ability to recognize that one has a mental illness, the capacity to label abnormal experiences as pathological, the specific attribution of one's symptoms to mental illness and willingness to accept help in the form of treatment.

Although classically associated with psychosis, insight can also be impaired in nonpsychotic illnesses, such as OCD, depressive disorders, eating disorders and even specific and social phobias. It impacts upon help-seeking and adherence in these conditions. The issue of insight is particularly challenging in anorexia nervosa where the body image distortions along with overvalued ideas about appearance and weight are held with a veracity that is akin to delusional ideation and has an impact upon well-being and behaviour that is similar to that with psychosis. While insight is primarily a medical term, ‘capacity’ is a related legal concept that reflects an inability to decide because of an impairment of the mind or brain. One’s level of insight can thus impact upon one’s legal capacity to decide about treatment or other personal matters.

7. Abnormalities of motor activity

Many psychiatric disorders and their treatments can result in disturbances to motor function that should be noted in the MSE, usually in the section that deals with appearance and behaviour. They may involve quantitative disturbances to the amount or speed of activity or can reflect qualitative deviations from normal motor activity. These alterations are important as in addition to providing clues to the diagnosis (e.g. psychomotor slowing in depression), on occasion they can reflect serious and potentially life-threatening pathology (e.g. muscular rigidity in neuroleptic malignant syndrome). Decreased motor activity is most commonly seen in depression, chronic schizophrenia and various organic mental disorders (e.g. hypoactive delirium). In depression, it classically involves combined slowing of mental and physical activity sometimes referred to as 'psychomotor retardation'. In chronic schizophrenia, the reduced activity can occur as part of the negative syndrome along with reduced motivation and social behaviour. It is important to consider the role of antipsychotic treatment through sedative effects and/or parkinsonism. In the latter, this may also be associated with cogwheel rigidity and mask-like faces. Stupor is an extreme form of motor retardation characterized by akinesia (loss or impairment of the power of voluntary movement) and mutism (inability to speak), which together are termed 'akinetic mutism' with preserved consciousness. Stupor can occur in a variety of conditions that include affective disorders, psychosis and organic brain disorders. Unlike comatose states, the stuporose patient retains some degree of responsiveness to external stimuli. Catatonia refers to an abnormality of movement and behaviour that relates to a disturbed mental state. It was commonly observed in psychiatry during the early and mid-20th century but is much less common nowadays, possibly because of the earlier treatment of mental disorders with effective antipsychotic interventions. It can involve a variety of unusual posturing and behaviours that may include repetitive or purposeless overactivity, or catalepsy (muscular rigidity and fixity of posture with reduced responsiveness to external stimuli, such as pain), resistance to passive movement and negativism (the tendency to either resist movement of a body part by another or to move in an opposite manner to a request, apparently without motive or purpose). In catatonia, the patient does not move normally despite the physical capability to do so. It is associated with schizophrenia, affective disorders, focal neurological lesions, intoxication and metabolic disturbances. The main features of catatonia are presented in table 7.

Increased motor activity can reflect anxiety, anger, agitation (e.g. agitated depression) or the hyperactivity of mania. Agitation or irritability may accompany many disorders (e.g. anxiety, depression, schizophrenia, organic disorders) and

reflect distress. In such cases, movement may not be goal-directed. In the hyperactivity of mania, actions are usually goal-directed, albeit frequently in response to disinhibiting thoughts or impulses and are not necessarily rational. Catatonic excitement may be seen in schizophrenia wherein the individual engages in non-goal-directed overactivity.

Table 7. Abnormalities of Motor Activity that can Occur in Catatonia

Catatonic Feature	**Description**
Posturing/catalepsy	The patient may maintain unusual and uncomfortable postures for extended periods; the psychological pillow is an example wherein the patient will hold their head above the pillow when lying down
Stereotypies	Nongoal-directed, repetitive movements
Mannerism	Seemingly goal-directed repetitive movements, but without any obvious purpose
Waxy flexibility	After being placed in an unusual position or pose, the patient will maintain this for an extended period
Automatic obedience	The patient will obey commands even when subsequently given instructions to the contrary
Echolalia	The patient repeats the speech of the examiner
Echopraxia	The patient repeats the actions of the examiner
Negativism	The patient will resist the examiners' attempts to make contact
Ambitendency	Alteration between resistance and cooperation

INTERNATIONAL CLASSIFICATION OF MENTAL DISEASES

The international classification of mental diseases (ICD-10) is not nosological since most of the the pathological conditions are considered to be in the framework of various disorders, which makes their genesis quite uncertain complicating development of their prognostic criteria. The classification consists of 11 sections, the following:

F0. Organic, including symptomatic mental disorders.

F1. Mental and behavioural disorders due to psychoactive materials use.

F 2. Schizophrenia, schizotypal and delusional disorders.

F 3. Mood (affective) disorders.

F 4. Neurotic, stress-related and somatoform disorders.

F 5. Behavioural syndromes associated with physiological disturbances and physical factors.

F 6. Disorders of adult personality and behavior.

F 7. Mental retardation.

F 8. Disorders of psychological development.

F 9. Behavioural and emotional disorders with onset usually occurring in childhood and adolescence.

F 99. Unspecified mental disorder.

Example

F08.82 Epilepsy

A seizure is a paroxysmal neurological event caused by the abnormal discharge of neurones. Epilepsy is defined as a tendency to recurrent seizures, that is two or more seizures. Epilepsy is not a single disease but it is a symptom of congenital or acquired CNS disease in the same way as weakness is a symptom in a range of different disorders. Different types of epilepsy can be classified according to different features, including seizure type, age of onset, prognosis and cause, and are more appropriately called the *epilepsies*. The epilepsies are the most common serious neurological diseases; 5% of the population will experience an epileptic seizure at some point in their life. Their prevalence is 0.5%; 370 000 people in the UK are affected. Males and females are similarly affected. Peaks of onset occur in childhood/adolescence in relation to congenital causes and in the elderly are presumed to be secondary to cerebrovascular and degenerative diseases. Seizures cause unpredictable loss of control, which makes epilepsy one of the most stigmatizing and socially disabling of all diseases, adversely affecting many aspects of life, such as increasing divorce rates, and adversely affecting employment opportunities. Epilepsy is associated with depression and psychiatric illness.

The diagnosis of epilepsy is clinical, depending on the history from the patient and, critically, from any witnesses of the attacks. This can be supported by investigations such as an EEG, but the main contribution of the EEG is in syndrome classification.

Classification of seizures and epilepsy syndromes. Much of the confusion about the classifications in epilepsy arise because of a failure to appreciate that there are two interrelated classifications: a classification of seizure type and a classification of epilepsy syndromes (table 8). Patients may have more than one type of seizure. The epilepsy syndrome includes diagnosis of seizure type and additional information, mostly relating to aetiology, including age, EEG and neuroimaging results. Where possible, patients' epilepsy should be classified by epilepsy syndrome rather than seizure type, which takes into account these other factors. The old terms 'petit mal' and 'grand mal' do not fit easily into this classification and should not be used.

Seizure types in focal and generalized epilepsies. Some seizure types occur only in focal or in generalized epilepsies but many can occur in both types and cannot easily be classified purely on the basis of clinical seizure type.

Table 8. Some of the more common epilepsy syndromes

Syndrome	Age of onset	Clinical features	EEG	Prognosis	Treatment
Childhood absence epilepsy (CAE)	3–12 years	Commonly in girls with many absences each day, mimicking daydreaming, rare convulsions	3 Hz spike and wave, often photosensitive	Usually remits in teens	Ethosuximide or sodium valproate
Juvenile absence epilepsy	7–17 years	Absences less frequent than CAE. Convulsions common	3 Hz spike and wave, rarely photosensitive	Good response to treatment, but may persist	Sodium valproate, ethosuximide, lamotrigine
Juvenile myoclonic epilepsy	10–20 years	Myoclonic jerks within first few minutes of waking and generalized tonic-clonic seizure also in morning Occasional absences	Polyspike and wave, sometimes photosensitive	Often persists but responds to treatment; worsens with carbamazepine	Sodium valproate, clonazepam, levetircetam
West syndrome	3–7 months	Flexor spasms, tonic and atonic seizures with half of development. Mental retardation usual	'Hypsarrhythmia'; mountains on EEG	Poor, especially secondary cases with, for example, tuberous sclerosis. Very severe epilepsy	Adrenocorticotrophic hormone and vigabatrin
Lennox–Gastaut syndrome	2–9 years	Tonic and atonic seizures and atypical absences	Slow spike and wave at 2–2.5 Hz	Persistent epilepsy and mental retardation common	Carbamazepine, sodium valproate, lamotrigine
Benign partial epilepsy with centro-temporal spikes (BECTS)	3–13 years	Occasional, motor seizures affecting one side of face, sometimes spreading. Usually nocturnal	Centrotemporal spikes, especially in sleep, shift between sides	Remits by age 20 years	Carbamazepine, often no treatment required

There are three broad categories of epilepsy syndromes:

1. *Generalized epilepsies* – are probably complex genetic traits causing abnormal excitability of thalamocortical circuits, creating diffuse, abnormal, synchronized neuronal discharges.

2. *Focal epilepsies* (localization related) – discharges arise from a specific, usually abnormal, cortical region that can either remain localized or spread more generally.

3. *Provoked seizures* due to acute abnormalities, e.g. trauma, metabolic abnormalities, drugs or alcohol.

Patients who have had only a few attacks may not be classifiable into an epileptic syndrome.

Generalized epilepsies. These usually start in childhood or adolescence and have typical clusters of seizure types, including tonic-clonic seizures, absences and myoclonic jerks, combined with a characteristic generalized EEG 'signature'. The most common forms are the idiopathic generalized epilepsies (IGEs), which represent well-defined clinical syndromes (table 9) and are not associated with structural brain disease. They generally have a good prognosis. There is a constitutional component with a significantly increased risk of epilepsy among family members.

Table 9. Symptoms of focal and generalized seizures

Seizure symptom	**Clinical significance**
Focal: Focal limb jerking; Focal tingling; Olfactory or gustatory hallucination; Visual hallucination; Limb posturing; Swallowing/chewing movements	Motor cortex onset; Somatosensory cortex onset; Temporal lobe onset; Occipital lobe onset; Supplementary motor area onset ; Temporal lobe/insula
*Generalized:*Generalized stiffening (tonic); Repeated generalized jerking (clonic); Intermittent symmetrical jerks (myoclonic); Absence with no focal symptoms Atonic drop attacks	

West syndrome and Lennox–Gastaut syndrome are rarer generalized epilepsies of early childhood; they have a much poorer prognosis and may be associated with mental handicap and structural brain disease such as tuberous sclerosis.

Focal epilepsy occurs at any age. The abnormal discharge appears to start in one part of the brain and may become generalized. The focal onset may be

reflected in focal symptoms at the onset of the seizure, indicating the abnormal region of cortex (table 9). The spread may be so rapid that the seizure appears to be a generalized convulsion from the outset and there are no early focal symptoms. There may be a post-ictal confusional state, during which the patient may wander and undertake stereotyped actions that appear purposeful ('automatisms'). These may include plucking at objects, or sometimes more sophisticated behaviours such as bed making or undressing. Without an EEG during the episode, this can be difficult to differentiate from complex partial status epilepticus (see below). An inter-ictal EEG (between seizures) may show localized spikes or sharp waves. This helps to support the diagnosis but their location does not always accord with the region of seizure onset. Focal epilepsy may be associated with focal structural brain disease. In younger patients, this is usually hippocampal sclerosis or developmental abnormalities of the cerebral cortex. Trauma, cerebrovascular disease and tumours are also common causes, especially in older patients. The prognosis for seizure remission and mortality is worse than in generalized epilepsies. The benign focal epilepsies of childhood, for example BECTS (see table 8), are relatively common focal epilepsies that usually remit in adolescence and are not associated with focal structural abnormalities.

Status epilepticus is defined as seizures occurring for 30 min, either continuously or intermittently, without recovery. It is a medical emergency (see below). The seizures may be:

- generalized convulsions (convulsive status epilepticus)
- simple, partial or focal, e.g. jerking of one side of the body (non-convulsive status)
- a confusional state, with or without abnormal motor activity (non-convulsive or complex partial status).

Investigation. An EEG is required to characterize the epilepsy but may be normal and this does not exclude a diagnosis of epilepsy. Repeating the EEG, especially with sleep deprivation, increases the diagnostic yield. In some cases, a prolonged, ambulatory EEG recording can 'catch' an attack, in which case it is helpful in diagnosis. Adults presenting over the age of 20 years should undergo a CT or MRI scan to exclude a focal structural lesion. The sensitivity of MRI is much greater for subtle developmental abnormalities but CT is adequate to exclude larger lesions, for example most tumours. Younger patients should be scanned if there is clinical or EEG evidence of focal seizure onset or if the seizures are proving difficult to control.

Single seizures. It is not uncommon to see patients who have had only a single seizure or cluster of seizures over a few hours or an unwitnessed blackout that was probably a seizure. A potential structural trigger should be sought by a CT or MRI brain scan in all patients with focal-onset seizures or in those over the age of 20 years. The advice following a single seizure is the same as for recurrent attacks (see below). The prognosis for recurrence varies according to the seizure type, cause and associated clinical features. Most that recur do so within the first year. Focal seizures recur more frequently, especially if associated with congenital lesions or tumours. Sixty per cent of convulsions recur by 1 year. However, if there has been an acute precipitant ('provoked attack'), for example acute alcohol withdrawal or a metabolic disturbance such as liver or renal failure, which is successfully treated, the recurrence rate is lower. The EEG is relatively unhelpful in determining the risk of recurrence. If the EEG is very abnormal, recurrence is somewhat more likely than if it is normal. Most clinicians do not treat a single seizure.

Advice following one or more seizures. Epilepsy usually causes a frightening and unpredictable loss of consciousness. The patient needs to understand the nature of the problem and the clinician needs to try to encourage the patient to live a normal life, at the same time understanding that there will have to be some restrictions for the patient's own safety and the safety of others. For example, the patient can continue to go swimming, but should be accompanied by a competent adult. Family members, employers and schools need to understand the diagnosis and how to deal with seizures. It is also the duty of the doctor to tell the patient that the Driving and Vehicle Licensing Authority (DVLA) must be informed of the condition. This is the case for all types of seizures, including single seizures and single provoked seizures. Current regulations are that a patient should be seizure-free for 12 months – from all types of seizures including partial, complex partial or myoclonic seizures. In provoked seizures, the DVLA may be more lenient but it must still be informed.

Epilepsy Diagnosis. Epilepsy is a symptom rather than a diagnosis in itself. There are different sorts of seizures and more than one type of seizure can occur in a patient. Epilepsy syndromes can be divided into generalized or focal-onset disorders.

Treatment and management – Neurology

When to treat? Most physicians would recommend treatment when a person has suffered two or more seizures within a 2-year period. The risk of recurrence

after a first seizure varies according to the aetiology and seizure syndrome and may influence the decision on when to treat.

Principles of medical treatment. Which treatment to use depends on the epilepsy syndrome, seizure types and adverse effect profile. One drug should be used, where possible, and the dose titrated against response and adverse effects. Sixty per cent of patients will respond to first-line therapy, becoming seizure-free for at least 2 years. Monotherapy carries the lowest risk of adverse effects, which increase substantially with increasing numbers of drugs. For most drugs, the correct dose is the lowest effective dose that does not cause side effects. A drug should not be considered ineffective until it has been tried to the maximum dose that does not cause adverse effects, which varies between patients. For refractory cases, more than one drug may be required and some will remain refractory to all agents. Using more than three drugs concurrently should be avoided. Some refractory cases, on re-evaluation, prove to have non-epileptic (psychogenic) seizures, also referred to as pseudoseizures. In others, poor compliance contributes to poor control. In refractory cases where these factors have been excluded, if there is evidence of focal seizure onset, surgery may be considered (see below).

Choice of medication.The major divisions into generalized and focal-onset epilepsies are important in the choice of drug. Medications can broadly be divided into those useful in focal epilepsy, those with a broad spectrum of action and those for specific seizure types. Carbamazepine, lamotrigine and valproate are the commonest first-line drugs in the UK. The choice is also heavily influenced by the age of the patient because this affects their susceptibility to the side effects of different drugs. For example, focal-onset epilepsy in a young woman is often treated with carbamazepine or lamotrigine as first line because of its lower risk of teratogenicity, but sodium valproate is favoured in the elderly because of a lower risk of ataxia and falls. Lamotrigine is emerging as a broad-spectrum drug, well tolerated in many patient groups.

This is of benefit in limited situations:

- In patients on polytherapy.
- Optimizing the dose of phenytoin and carbamazepine.
- In the assessment of compliance.

In judging drug dosage, blood levels are most useful for patients on phenytoin therapy. The saturation kinetics of this drug give it a particularly narrow therapeutic window. There is substantial variability between patients. There is some value in measuring drug levels in patients receiving carbamazepine or

barbiturates but little benefit for other drugs apart from finding out whether the patient is taking them (e.g. unconscious patient).

Adverse effects. The adverse effects of antiepileptic drugs are common and major adverse effects are listed in table 10. Sedation can occur with all drugs and is the most common complaint, especially with polytherapy. Another concern is teratogenicity. Women of childbearing age on antiepileptic medication should be counselled of the risk and their medication minimized prior to conception. Although not proven to be of benefit, folic acid supplements (5 mg daily) are generally prescribed to women of childbearing age taking antiepileptic drugs as it may help to prevent neural tube defects. The risk of major malformations for a woman taking anticonvulsants is about 4–9%, compared with about 1–2% in the general population. It is highest for those on valproate and on multiple drugs.

Table 10. Selected adverse effects of anticonvulsant drugs

Adverse effect	Drugs
Sedation	All drugs, especially phenobarbital and benzodiazepines Substantial individual variation
Diplopia and ataxia	Phenobarbital, phenytoin, carbamazepine, lamotrigine
Rash	Carbamazepine, lamotrigine, phenytoin
Gastrointestinal effects	Carbamazepine, sodium valproate
Weight gain	Sodium valproate, vigabatrin, gabapentin, pregabalin, others infrequently
Weight loss	Topiramate, zonisamide
Reversible hair loss	Sodium valproate, vigabatrin
Teratogenic effects	Proven for carbamazepine (safest), phenytoin, phenobarbital, clobazam, sodium valproate, topiramate Unknown for other new drugs
Visual field loss	Vigabatrin (rarely used as a result)

Drug interactions. Carbamazepine, phenytoin and phenobarbital are potent liver enzyme inducers. They increase the rate of elimination of the contraceptive pill so that a higher-dose pill needs to be taken to compensate. They also increase the metabolism of other drugs eliminated via the liver, including other antiepileptic drugs. Sodium valproate inhibits liver metabolism of some drugs. The drug most sensitive to these effects is lamotrigine; its half-life varies from 12 h (with concurrent enzyme inducer) to 70 h with concurrent sodium valproate. The new

drugs gabapentin, topiramate and levetiracetam are principally renally excreted so interaction is less of a problem.

When to stop treatment. In general, the same factors that predict seizure recurrence are also associated with relapse on cessation of treatment. If medication is withdrawn after 2 years of being seizure-free, there is a risk of recurrence of 25–40%. There is no absolute predictive test, and seizure recurrence is always less if patients continue with treatment than if they stop. For this reason, the decision to stop treatment is largely a personal one. For example, a woman who wants to start a family may accept a recurrence of partial seizures if it means that her baby is not exposed to the teratogenic effects of drugs *in utero* , but a travelling salesman may wish to continue with medication indefinitely, rather than increase the risk of losing his driving licence.

Surgical treatment of epilepsy. Patients with focal-onset seizures not controlled by drugs should be considered for neurosurgical treatment. Before undertaking surgery, the epilepsy must be demonstrated to come from a single part of the brain that could be removed, without leaving any major neurological deficit. It requires detailed MRI studies, EEG recordings, including recordings of seizure onset (sometimes with intracranial electrodes) and neuropsychological assessment to establish the risks of surgery for cognitive function. The forms of epilepsy most amenable to surgical treatment are temporal lobe epilepsy due to mesial temporal sclerosis and epilepsy due to foreign tissue lesions.

Prognosis of established epilepsy. The natural history of epilepsy is poorly understood. The prognosis for remission depends on the epilepsy syndrome and is generally good. Most generalized epilepsies remit in adolescence or early adult life, except juvenile myoclonic epilepsy which usually persists. Partial epilepsy syndromes, especially those with a congenital cause, are usually more persistent, but 80% of these also achieve a 3-year remission by 9 years after onset. The EEG is of little value in determining prognosis in most cases.

Epilepsy mortality.The mortality of patients with epilepsy is up to three times that of age-matched controls. The increase is seen mostly in focal epilepsies. Some of this excess is due to the underlying cause of the epilepsy, for example tumours, and some is clearly due to seizure-related events, for example status epilepticus or drowning. There remain patients who die suddenly probably following a seizure. This is called sudden death in epilepsy and may affect up to 0.5% of epilepsy sufferers per year. The likely causes are apnoea or fatal cardiac dysrhythmias due to unwitnessed seizures.

Management of status epilepticus. Status epilepticus is a medical emergency and convulsive status epilepticus (CSE) is life-threatening. CSE causes a variety of secondary manifestations, including hypoxia, acidosis, myoglobinuria, renal failure, disseminated intravascular coagulation and hyperthermia. Most of these complications reverse rapidly on cessation of seizures but, untreated, the mortality is high.

Treatment is directed to: general resuscitation; stopping the seizures; treating the underlying cause.

Patients fall into two general categories: those with a previous diagnosis of epilepsy and those presenting for the first time, in whom serious new disease underlying the seizures is likely . The cause may be metabolic dysfunction, drugs, intracranial mass lesions, haemorrhage or infection. These patients need to be investigated for metabolic disturbance, undergo urgent neuroimaging and, if this is normal, CSF analysis, especially to look for encephalitis. An EEG may also help with this diagnosis. Treatment should be initiated immediately to stop the seizures and to prevent further seizures. In general, if the seizures stop, most of the secondary metabolic abnormalities will correct rapidly. First-line treatment is a benzodiazepine (lorazepam or diazepam intravenously or rectal diazepam) then a loading dose of 10–15 mg/kg of phenytoin given by intravenous infusion.In patients with a known history of epilepsy, drug withdrawal seizures should be considered and urgent anticonvulsant blood levels obtained. If there is drug withdrawal, the same drug should be restored if possible, otherwise treatment should be along the same lines as with *de novo* cases. If patients with known epilepsy respond rapidly to treatment, such intensive investigation may not be required, but if they do not respond, investigation should proceed as above. If patients do not respond rapidly to treatment, the diagnosis should be reconsidered. If seizures are not controlled, the patient should be entubated and ventilated and given thiopental. EEG monitoring is needed to monitor control of seizures. Many cases of ‘refractory status’ turn out to have psychogenic seizures, rather than epilepsy, but this is a difficult diagnosis and requires specialist advice.

Treatment and management:

- ▪ Choice of drug depends on the epilepsy syndrome and adverse effects.
- ▪ Monotherapy should be used if possible.
- ▪ Some drugs interfere with the oral contraceptive pill or are teratogenic.
- ▪ Status epilepticus is a medical emergency.

Instructions for carers witnessing a convulsive seizure:

- Remove any objects on which the individual may harm themselves.
- Put the patient into the recovery position.
- Call an ambulance if convulsion lasts longer than 10 min.
- Do not try to put anything into the patient's mouth.
- Do not try to restrain the convulsion.
- If the person wanders after the convulsion, gently guide them to safety; do not try to exercise restraint.

F78.9 Intellectual Disability

1. You have been asked to assess Larry, a 34-year-old man with Down syndrome. He lives with his elderly parents and attends 'An Sli Eile', a local day service for people with intellectual disability. Over the past few weeks, Larry has had daily episodes of irritability, tearfulness and agitation. He is also reported to have disturbed sleep, reduced appetite and episodes of shouting, which is out of character for him. When asked by his parents or care staff what is wrong, Larry repeatedly replies with the word 'sad'.

- 1. What are the general principles of assessment when assessing a person with an intellectual disability?
- 2. What historical information would be important to establish in this case?

When assessing a person with an intellectual disability, it is always important, as with any clinical assessment, to obtain an accurate and careful clinical history. Many people with an intellectual disability can give a good history, but some cannot. Therefore, these people depend on their family or paid caregivers to give as accurate a collateral history as possible. People with an intellectual disability must be supported at clinical examinations and assessments by family or support staff who know them well. The ability of people with an intellectual disability to give a good history will depend on their verbal skills and their level of intellectual disability. Many people with an intellectual disability report that family or support staff frequently talk about them at hospital or clinical appointments as though they are not present, or that they talk about upsetting things in front of them. Therefore, always remember to introduce yourself to the patient and ask them if they would like to see you alone or if they would prefer family or support staff present. It is also important to remember that an assessment of individuals with an intellectual disability and mental health problems takes

longer than those who do not have an intellectual disability. Therefore, patience and understanding are important.

Relevant historical information includes the following:

Recent life events: Explore for any significant events (especially losses) in Larry's family and social pool.

Medical history : Has Larry had any cardiac problems, e.g. ventricular septal defect, atrial septal defect? Is there a history of seizures or gastrointestinal problems, e.g. hiatus hernia, gastritis or constipation? Has he had any thyroid problems–hypo or hyperthyroidism?

Surgical history : Has Larry had any past or recent surgery (e.g. cardiac)?

Psychiatric history : Have there been any other behavioural or mental health issues or similar episodes in the past?

Medications : Is Larry taking any regular medications?

Family history : Is there any family history of mental health problems, e.g. mood disorders, schizoaffective disorders, schizophrenia or addiction.

Premorbid personality : Try to ascertain what Larry's personality was like before this. Ask Larry or his family member/caregiver to describe this if possible. What are his interests and hobbies? Who are his friends? What type of work does he do? Have these been affected by the current change in Larry? Has he had any recent difficulties with his memory or any episodes of confusion?

Social history : Ascertain the home circumstances and details of support available to Larry and his parents.

2. Collateral information from Larry's parents and his records indicate that he has an intellectual disability in the low–moderate range, and that he has grand mal epilepsy and has been seizure-free for three years. He also has a history of hypothyroidism. He has no significant psychiatric history. Larry had a ventricular septal defect repaired when he was four years old, and he had frequent hospitalizations in his early years, mainly because of his cardiac condition. All major developmental milestones were significantly delayed, and he attended a local school for children with intellectual disabilities from age six until 18 years. He then transitioned to the current day centre. Larry has two older siblings living abroad who visit annually.

Larry's current medications are as follows: sodium valproate (300 mg; twice a day) for seizure prophylaxis and L-Thyroxine (50 μg; daily). He attends the day

centre three days per week for six hours and generally enjoys this. In the last few weeks, the staff at the day centre have reported that Larry has been very talkative, restless and fidgety, with poor concentration in the tasks that he previously performed with ease.

- 3. Why is Larry's medical history of particular relevance?
- 4. What is your differential diagnosis at this stage?

Further reading **For a review of the prevalence of health conditions in intellectual disability, see:** Oeseburg B, Dijkstra GJ, Groothoff JW, et al. (2011) Prevalence of chronic health conditions in children with intellectual disability: A systematic literature review. Intellectual and Developmental Disabilities 49(2):59–85. doi:10.1352/1934-9556-49.2.59

Both hypothyroidism and epilepsy can affect a person's mood and behaviour, along with the medications used to treat these conditions. People with Down syndrome have an increased prevalence of both congenital and acquired hypothyroidism. The lifelong prevalence has been reported as ranging from 13% to 63% (this is approximately 4% in the general population). The prevalence of epilepsy among those with an intellectual disability is higher than that in the general population. Community-based studies of epilepsy in adults with an intellectual disability show a prevalence of 16%–26%. Some studies have shown a higher rate of behavioural and psychological problems in those with epilepsy than those without epilepsy. However, other studies have not shown this trend. There is also an increased rate of psychiatric illness among adults with an intellectual disability, which has been reported to be between 15% and 40%.

The differential diagnoses at this stage include the following:

• Situational or adjustment difficulties with challenging behaviour
• Affective disorder, e.g. depression, mixed affective state, manic episode
• Severe anxiety disorder
• Psychotic disorder
• Organic disorder, including substance use and delirium.

3. Larry has been distractible and reluctant to follow advice or requests. He has been tearful on several occasions during the day and is persistently complaining of sadness or distress. Larry has not shown any challenging behaviour (verbal or physical aggression, or any self-injurious behaviour) at home or in the day centre but has required a high level of support and redirection from staff in the centre and his parents at home. He has difficulty getting off to sleep, with recurrent episodes of waking and pacing throughout the night. The behaviours described are

markedly different from Larry's usual pattern as he normally engages very well with his daytime routine. He has not expressed any suicidal thoughts or ideas of self-harm. Larry did not have any distressing or similar behaviour or mood change at home or in the day centre prior to this episode. Larry has no history of substance misuse and has not attended mental health services in the past or been prescribed psychotropic medication. Larry's physical health was described as good at his annual health check, which was undertaken by his general practitioner one month ago. He underwent routine blood tests, the results of which were reported as unremarkable.

- 5. What are the diagnostic criteria for intellectual disability and how is intellectual disability classified?
- 6. What is the prevalence of intellectual disability?
- 7. What are the models of service delivery for those with an intellectual disability?
- 8. What do you know about the cause of intellectual disability?

The diagnosis of intellectual disability is applied in cases of the following:

1. Evidence of functional impairment on intellectual functions (comprehension, learning, problem-solving, planning, abstract thinking and judgement) that is evident with formal testing.

2. There is impaired socio-adaptive function secondary to these intellectual impairments.

3. Impairments are evident during development and are typically present from birth/early childhood and are persistent over time and consistent over domains of activity.

Intellectual disability is classified in several ways that include consideration of the intelligence quotient as well as social and adaptive or functional abilities as outlined in table 11.

Table 11. Classification and Prevalence of Intellectual Disability

	IQ [a]	**Social and Adaptive Abilities**	**Prevalence**
Mild	50–69	Delayed speech Independent Academic difficulties Mental age: 9–12 years	3%
Moderate	35–49	Deficits in language comprehension difficulties Requires supervision Mental age: 6–9 years	0.3%
Severe	20–34	Motor deficits and associated disabilities Limited language that impedes communication Requires help with ADL Mental age: 3–6 years	0.1%
Profound	< 20	Very limited language and comprehension Severe neurological and physical disability, immobile, incontinent Mental age <3 years	0.05%

a Clinical judgement should be exercised in the interpretation of IQ tests. IQ, intelligence quotient; ADL, activities of daily living

Historically, because of social stigma at the time, many people with intellectual disabilities were removed from their families, often at a very young age, and were cared for in residential homes for people with disabilities or in psychiatric hospitals. Intellectual disability services in Ireland were run by religious organizations or state-run institutions. In recent years, the model of service has been changing and is becoming a community or home-based service, which is more person-centred. Employment and vocational training and day centres with the support of specialist multidisciplinary intellectual disability teams are now being developed. Education is based on ability; it needs and includes mainstream or special education schooling options.

There are multiple potential causes of intellectual disability. However, a specific reason is identified in about 25% of cases

4. Larry attends an appointment at the local mental health clinic. He is accompanied by his parents and a key worker from his day service. On the mental state examination, Larry is observed to be restless and agitated and does not sit down or stay still for very long during the appointment. He is somewhat amenable to reassurance from the care-worker who accompanies him. He does not engage in conversation very well and repeatedly repeats the word 'sad' during the appointment. Larry repeats this word in response to most questions posed and does not give expansive answers to many of the questions asked. Larry does not appear to be experiencing hallucinations in any modality. He is fully conscious and alert and does not appear disorientated. Psychomotor activity is increased and Larry is tearful and labile in his affect. He does not describe any suicidal thoughts or thoughts of self-harm.

- 9. What does the psychiatric assessment of a patient with an intellectual disability entail?
- 10. What further assessments and investigations would be relevant, given the information thus far?
- 11. What other people involved in Larry's care could be good sources for collateral information?
- 12. What do you know about the epidemiology of mental illness in patients with an intellectual disability?

The principles of psychiatric assessment in those with an intellectual disability involve establishing the pattern of symptomology and changes in behaviour. The impact of their intellectual disability on symptoms needs to be

established. Close observation of appearance and behaviour, serial assessments and assessment in the patient's natural environment may be important.

A full physical examination should be carried out by the general practitioner (GP) prior to the mental health assessment. The GP may carry out routine bloods as clinically indicated, i.e. in Larry's case, thyroid function test, valproic acid levels (to rule out valproate toxicity), full blood count and urea and electrolytes should be prioritized. Given Larry's preexisting conditions, a computed tomography brain scan, electrocardiogram or echocardiogram may be clinically helpful depending on the findings on physical examination. It may be helpful to refer to any existing psychological, social work, occupational therapy or speech and language assessments.

Other potential sources of collateral information would include day service managers, other day centre staff and support workers, Larry's GP, family members, who although abroad may still have clinically relevant input and also respite staff who may have important information relating to Larry's premorbid state.

All categories of mental illness occur in people with intellectual disabilities, and many disorders are more common. For example, people with an intellectual disability are four times more likely to suffer from depression or anxiety. The prevalence of schizophrenia is three times higher, and bipolar affective disorder is also more common.

5. The physical examination is unremarkable apart from the presence on auscultation of Larry's preexisting cardiac murmur. Larry's valproic acid level is in the subtherapeutic range, and his full blood count, urea and electrolytes and thyroid function tests are normal. The electrocardiogram is normal, and brain computed tomography, electroencephalogram and echocardiogram are requested. Referral to neurology is also requested as Larry has not attended a review appointment for approximately two years.

Having carefully considered Larry's history, mental state examination results, and collateral information, together with physical examination and investigations, you make a diagnosis of a mixed affective episode. You liaise with the consultant psychiatrist in intellectual disability who concurs with your diagnosis. You draw up a management plan together. Prompt treatment is a priority. After phlebotomy, you increase Larry's sodium valproate up to 500 mg orally twice daily and prescribe a low dose of antipsychotic–olanzapine or quetiapine. You also prescribe an as-needed medication for severe agitation or in

the event of symptoms not resolving (lorazepam or an antipsychotic). You plan to follow-up on the investigations requested to rule out a potential organic cause.

- 13. Can you explain the logic behind the medication changes?

In the treatment of an acute manic episode, the optimization of medication used for mood stabilization is paramount. Sodium valproate is widely used as a mood stabilizer and has shown efficacy in rapid-cycling bipolar affective disorder. It may be possible to titrate up the dose of this medication because Larry is already receiving it for epilepsy, and because it appears effective in preventing seizures. Plasma levels of valproate are less precise in terms of defining its therapeutic range in epilepsy than lithium levels are for a mood-stabilizing effect.

As Larry is presenting with agitated behaviour, in the acute phase, the use of short-term benzodiazepines such as clonazepam may be useful in reducing agitation and improving sleep. Alternative benzodiazepines to clonazepam, such as lorazepam or diazepam, may be considered. Alternative mood-stabilizing medications could also be considered in this situation as first- or second-line treatments. These alternatives include the use of atypical antipsychotics, lithium, carbamazepine, lamotrigine and other antiepileptic medications. When prescribing psychotropic medication, it is extremely important to consider their potential effect on seizure threshold (e.g. this is usually lowered by antipsychotics) and the psychological side-effect profile.

6. You arrange a case conference/multidisciplinary team meeting and invite Larry's parents to attend. You have previously explained to Larry's parents that you and the consultant have concluded that Larry is experiencing an episode of mood disturbance and that you have decided to change Larry's medications. You recommend that Larry avail of respite if it is available. You discuss the possible pros and cons of the changes to Larry's medications and your reasoning behind the changes. You also draw up guidelines around when it would be appropriate to administer the as-needed medication. You also explain that further investigations have been requested to rule out other potential causes. The social worker attached to Larry's day service proposes that he will liaise with Larry and his family regarding the arrangements for respite. The respite manager is also present at the case conference and, given the circumstances, agrees to facilitate acute respite for Larry but outlines that respite resources are very limited within the service, and that only short-term respite will be possible.

- 14. What chromosomal abnormalities can occur in Down syndrome and how does prevalence increase with maternal age?

- 15. What are the clinical features of Down syndrome?

Down syndrome is the most common genetic cause of intellectual disability. Furthermore, 95% of Down syndrome cases are associated with the nondisjunction of chromosome 21 (trisomy 21), with 75%–85% of nondisjunction's being maternal in origin. Approximately 5% of Down syndrome cases are as a result of a Robertsonian translocation, and 1%–3% is associated with mosaicism. The risk of Down syndrome increases with maternal age; in the <30 years age group, its prevalence is 0.7 per 1000, rising to 35 per 1000 in those over 45 years. Clinical features of Down syndrome include: short stature; small head, ears and mouth; a protruding tongue, broad neck, epicanthal folds, congenital heart defects, hearing deficits, strabismus, oesophageal atresia, Hirschsprung's disease, obesity, hypothyroidism and epilepsy.

7. Unfortunately, Larry cannot be facilitated in his usual respite house and is admitted to one nearby instead. The plan is for daily assessment by the consultant psychiatrist or nonconsultant hospital doctor. For the first two days, Larry's symptoms remain largely unchanged with the persistence of insomnia and agitation. This presents significant management difficulties for staff, particularly at night, and some residents who are staying for planned respite are distressed by Larry's behaviour. You titrate Larry's sodium valproate up to 800 mg orally twice daily to stabilize Larry's mood. A repeat plasma valproic acid tests is ordered as this increase is in the mid-therapeutic range. Larry's sleep improves on the fourth day of respite and his degree of agitation reduces. He requires frequent lorazepam during his first five days of respite. Larry's lability of affect dissipates at day five, and he becomes less restless and does not have repetitive speech anymore. He continues to express that he 'feels sad'. After one week in respite, the respite manager contacts you and asks if Larry's care could be continued with management in the community. You agree to a trial of community management under close supervision. The social worker agrees to liaise with Larry's family regarding these arrangements and support from the community mental health nursing service is also arranged.

Larry's father enquires about the possibility of residential placement for Larry and cites his own and his wife's ages as the reasoning behind this. He says that even prior to this episode, they were having significant difficulties in assisting Larry in his activities of daily living because of their physical limitations. You state that you will present a report to the residential admissions committee citing Larry's parents' concerns together with your clinical opinion. You will also ask the occupational therapist to visit the home and reassess Larry's activities of daily

living needs. Larry's symptoms settle over the next four weeks and he returns to his baseline state. The results of awaited physical investigations are normal. Larry returns to his day centre placement. There are no indications of functional change or cognitive decline from his premorbid state. However, you still feel it is prudent to arrange a cognitive assessment for Larry. You also request regular periods of respite for Larry. You advise the team that Larry is likely to require more home resources as time advances. Given Larry's age, he is at a high risk of developing Alzheimer's-type dementia in the future. You arrange for Larry to have regular follow-up psychiatry appointments in the future.

- 16. What would a cognitive assessment involve?
- 17. What are the general principles of management in patients with an intellectual disability?

Cognitive testing can be achieved using a specific scale for people with Down syndrome called the Down syndrome dementia scale along with other formal tools and a baseline assessment of functional abilities, mobility and language skills. Establishing a history of changes in cognitive ability is important. It is important to exclude psychiatric disorders, e.g. depression and organic disorders, e.g. hypothyroidism or delirium, as these can present with cognitive problems.

Further reading **For a review of cognitive testing and dementia in Down Syndrome, see:** Hithersay R, Hamburg S, Knight B, Strydom A. (2017) Cognitive decline and dementia in Down syndrome. Current Opinions in Psychiatry 30(2):102–107. doi:10.1097/YCO.0000000000000307

Estimates suggest that ≥50% individuals with Down syndrome will develop Alzheimer's dementia as they age. This is linked to the activity of chromosome 21, which carries the amyloid precursor protein (APP) gene, which codes for the APP protein, and can lead to beta-amyloid plaque formation in the brain. Symptoms often occur earlier than in the general population, typically beginning in the 50s or 60s. The risk of someone with Down syndrome developing dementia increases from 20% at the age of 50 years to 80% by the age of 65 years.

Management principles in dealing with individuals with an intellectual disability include the following:

- The use of multidisciplinary teams
- Community inclusion as an important aspect of management to allow individuals with an intellectual disability to feel they have a valued social role with dignity and respect

- Psychological interventions, including behavioural therapies, cognitive behavioural therapy, family education, therapy or psychodynamic therapies, e.g. relaxation therapy, art, drama, and music therapy, are frequently available and therapeutic
- Treatment of underlying mental illness
- When prescribing, it is important to use a 'start low go slow' approach and give due consideration to the following:
    - Increased or reduced sensitivity to therapeutic effects
    - A higher rate of adverse effects
    - Increased sensitivity to side-effects of medications.

F08.8 Dementia

1. Eric is a 71-year-old retired health, safety and environment administrator who has been a widower since his wife died 18 months ago. His daughter contacts you, his general practitioner, to arrange a consultation because she is concerned that in the last 6–12 months, he has 'not quite been himself', and in particular, has seemed forgetful at times, mixing up his grandchildren's names.

- 1. What are your initial thoughts regarding the possible explanations for this presentation?
- 2. What additional information might you seek?
- 3. How can you assess his current level of cognitive functioning?

Memory and other cognitive problems in older people are often minimized and attributed to 'old age', by both the individual and their family. Furthermore, the individual may be seemingly unaware of the cognitive problems, and family members may be the ones who initiate presentation for assessment. The loss of a spouse or close supporting relative may expose the cognitive problems in an individual, in that a spouse may have been supporting and compensating for memory and other cognitive problems in the affected individual. Key elements of the initial assessment include a history of the nature, duration and progression of the cognitive difficulties, baseline cognitive function and comorbid medical and psychiatric disorders. As with other areas of psychiatric assessment, obtaining a comprehensive collateral history from family is vital, focussing on the key cognitive domains, along with an assessment of any functional loss. Several brief cognitive screening measures. These assessments can be easily conducted by a general practitioner (GP) or at a psychiatric clinic. Abnormalities on these initial assessments may lead to a specialist referral to old age psychiatry, neurology, geriatric medicine or a memory/cognitive assessment clinic for further more

detailed neuropsychological testing that may need to be repeated over a one to two year period to check for any evidence of change or progression in the cognitive deficits.

2. With further questioning, Eric's daughter tells you that he has started to become flustered when out driving ever since new traffic lights were installed at the end of his road, that he has stopped attending mass each morning, which had been his usual routine, and that he recently switched from the cryptic to the simple crossword in the *Irish Times* newspaper. Eric himself seems unworried and explains that his daughter 'has always been a bit of a fusspot'. On formal testing, his mini-mental state examination score is 25/30.

- 4. What is the normal range for the mini-mental state examination? What are the main differences between the mini-mental state examination and the Montreal cognitive assessment?
- 5. What additional brief cognitive tests might be useful to assess his attention, executive function, recent memory and visuospatial function?
- 6. What is mild cognitive impairment and how is it defined?

Further reading **For a review of cognitive assessments, see:** Young J, Meagher D, MacLullich A. (2011) Cognitive assessment of older people. The British Medical Journal 343:d5042. doi:10.1136/bmj.d5042

How do we assess cognition at the bedside/in clinic?

• Both the mini-mental state examination and Montreal cognitive assessment test allow for testing of a variety of cognitive domains and have cut-off scores that are linked to significant cognitive impairment. Note that both tools are subject to restrictions regarding their use in terms of cost and training, respectively.

• The clock drawing test is also sometimes used as a general test of cognition as it tests executive function, planning, memory and visuospatial awareness.

• Otherwise, single tests can be used for specific cognitive domains, such as the months backward test for attention, remembering named items over 3–5 minutes (short-term memory) and listing words that begin with 'F' or types of animals (executive function).

Mild cognitive impairment (MCI), which is also referred to as 'mild cognitive disorder' in the International Classification of Diseases-10 and 'minor neurocognitive disorder' in the Diagnostic and Statistical Manual of Mental Disorders (DSM)-5 involves (despite the name) significant cognitive impairment

on one or more domains that occur in the absence of significant functional impairment. It is the absence of functional impairment that distinguishes MCI from dementia. A detailed assessment of everyday routines and activities is needed to identify functional impairment. In previously high functioning individuals, declining function may be subtle (e.g. moving to a simpler crossword type). With the progression of dementia, there will be increasing evidence of deficits in physical self-maintenance (e.g. self-hygiene, dressing), in addition to the (generally earlier) decline in everyday activities (e.g. driving, cooking, engagement with social activities). Individuals with MCI have a 10-fold increased risk of progression to dementia in the subsequent year. The pattern of deficits on testing in MCI may also suggest future dementia subtype; for example, amnestic deficits suggesting a relatively higher risk of Alzheimer's dementia.

3. Eric's daughter wonders if he should have a 'brain scan' and tells you that he was a heavy smoker until his late 50s when he developed angina, and that he was also commenced on a statin for high cholesterol. He had an operation to remove a nodule from his thyroid gland 30 years ago.

- 7. What physical conditions might relate to his presentation and what are the causes of the so-called 'reversible dementia?'
- 8. What investigations would you perform?

Diagnosis of neurocognitive disorder (dementia and mild cognitive impairment):

• Evidence of significant decline from a previous level of performance in one or more of the following cognitive domains: learning and memory, language, executive function or social cognition. These deficits are evident with formal testing.

• In major neurocognitive disorder, the cognitive deficits are of a severity that they impact upon independence in everyday functioning, for example, self-care and managing personal affairs. In minor neurocognitive disorder, everyday functioning is relatively preserved and does not require assistance from others.

• The cognitive deficits are sustained and typically progressive over time.

• Cognitive deficits are not better explained by another mental disorder (e.g. delirium, depressive illness).

Eric's vascular risk factors (history of heavy smoking, angina and dyslipidaemia) are risk factors for vascular dementia, Alzheimer's dementia and dementia of mixed vascular/Alzheimer's aetiology. The identification and tight

control of vascular risk factors are important at a primary and secondary prevention level in the treatment of MCI and dementia. Thyroid dysfunction (perhaps relevant in this case) may also present with cognitive deficits (e.g. cognitive slowing and memory problems in hypothyroidism).

Other routine blood screen measures include a full blood count, renal function, liver function, vitamin B12, folate, erythrocyte sedimentation rate, C-reactive protein and fasting glucose. Identification and treatment of abnormalities in these measures may not necessarily reverse dementia, but appropriate treatment may nevertheless lead to improvements in general health and subsequent cognitive health.

Along with the blood screen measures outlined above, additional health screening measures (and potential contributors to cognitive impairment) should be taken, including syphilis serology, human immunodeficiency virus testing, calcium screen, chest X-ray and electrocardiogram (ECG).

In addition, neuroimaging is an essential component of the screening and workup process. Computed tomography or (preferably) brain magnetic resonance imaging can reveal potentially treatable causes of cognitive impairment (e.g. tumour or normal pressure hydrocephalus). It can also indicate the level of cardiovascular disease and any significant morphological changes, such as cortical atrophy and ventricular enlargement.

The dementia screening and workup process can thus be seen to have three primary functions. First, potentially reversible and treatable causes of cognitive impairment can be identified and managed. Second, managing comorbid health problems in an individual with dementia or MCI may lead to improvements in their general and cognitive health and potentially delay cognitive deterioration. Third, baseline cognitive and physical testing is important in tracking the progress of dementia and in monitoring treatment response.

4. His daughter is also concerned that Eric has seemed less energetic and withdrawn in recent times. Having stopped going to mass this year, he has not accompanied his friends on their usual weekend fishing trips. She says that he is easily upset and seems less confident in himself. She wonders if he might be depressed.

- 9. How can you clarify if he has clinical depression?
- 10. What is the relationship between mood disorder and cognitive difficulties in the elderly?

Depression is common in established dementia and may occur in up to half of the cases. Depression in earlier or mid-life may also be a risk factor for cognitive impairment and depression later in life. The diagnosis of depression in dementia may be more complicated than in non-dementia populations because of the overlap between certain depressive and dementia-related features (e.g. apathy, withdrawal and functional impairment). The key to diagnosis is a detailed history, collateral history and mental state examination, focussing on biological symptoms of depression and subjective reports from the patient and family of emotional and behavioural changes. When diagnosed, depression should be treated as it would be in non dementia populations, with serotonin specific reuptake inhibitors or serotonin and noradrenaline reuptake inhibitors. Tricyclic antidepressants should be avoided because of their anticholinergic side-effects and potential to worsen cognitive function.

5. Upon questioning, it is apparent that Eric does not have evidence to indicate any sustained lowering of mood or change to his usual energy, sleeping patterns or appetite. He still enjoys things but is worried that he might get mixed up doing things or become lost when he goes out, as this has happened once or twice. In addition to his vascular risk factors, he tells you that he has an older brother who has been in a local nursing home for the past four years 'with Alzheimer's' (G30, F00).

- 11. What are the different types of dementia and how are they relevant to treatment and prognosis?
- 12. How can they be distinguished in clinical practice?

Alzheimer's dementia (AD) accounts for half to two-thirds of the cases of dementia, with vascular dementia accounting for at least one-quarter. Improved neuroimaging in recent years has led to increased diagnoses of mixed Alzheimer's and vascular dementia. Less common types (e.g. dementia with Lewy bodies [DLB], frontotemporal dementia [FTD] and Creutzfeldt–Jakob disease) account for 5%–15% of dementia cases overall. Key aspects of the history (nature and progression of cognitive deficits) and cognitive profile may help elucidate the dementia subtype with blood tests and neuroimaging providing further clarification.

The cognitive deficits seen in AD tend to be predominantly related to short-term memory in the early stages and progress slowly over time. Traditionally, cognitive deficits in vascular dementia are described as having a stepwise progression, with abrupt drops in cognitive function followed by plateau phases. In

clinical practice, this distinction is not always clear, especially in cases of mixed aetiology.

DLB may have one or more of a characteristic triad of fluctuating cognitive profiles, Parkinsonism and visual hallucinations, thus making a distinction from delirium difficult at times. FTD often presents with changes in personality and behaviour. There may be a 'disinhibited' presentation with elements of disinhibition and coarsening of personality and behaviour and/or an apathetic presentation with social withdrawal. Generally, in FTD, there is a notable lack of insight/awareness in the patient and relatively preserved performance on standard cognitive testing (e.g. mini-mental state examination [MMSE]) at least in the early stages.

While acetylcholinesterase inhibitors (donepezil, rivastigmine and galantamine) are not disease-modifying, they are indicated early during dementia and may have a symptomatic role in AD, vascular, mixed AD/vascular dementia and DLB. The mode of action of these drugs is to increase acetylcholine levels through inhibition of acetylcholinesterase. All three agents are available in an oral formulation, and rivastigmine has an additional transdermal patch formulation. No agent is clearly superior in terms of efficacy or side-effect profile. Given the absence of a cholinergic deficit, these drugs are not indicated in FTD.

Donepezil has the longest half-life (70 hours) and, therefore, can be used on a once-daily basis. Modest short-term improvements in cognition and clinician ratings have been demonstrated, with additional benefits at the 10 mg dosage than the starting 5 mg dosage. The most common side-effects are related to peripheral cholinergic activity and include nausea, vomiting, diarrhoea and anorexia. Pulse (and an ECG) should be checked before starting acetylcholinesterase inhibitors as they can cause syncope because of cardiac effects, particularly, in those with supraventricular conduction abnormalities. Rivastigmine has effects on both acetylcholinesterase and butyrylcholinesterase, although the latter is clinically insignificant. Its side-effect profile is similar to donepezil and galantamine. Rivastigmine tends to be the agent of choice in Parkinson's disease dementia and DLB. Galantamine has a half-life intermediate between that of donepezil and rivastigmine. Its side-effects and efficacy profile are similar to those of the other two agents.

Memantine (an N-methyl-D-aspartate receptor antagonist) has a potentially symptomatic role in moderate to severe dementia of Alzheimer's and vascular aetiology. The effect is mediated through its anti glutamatergic and, thus,

potentially, neuroprotective action. In practice, acetylcholinesterase inhibitors and memantine are frequently used together from the early stages and throughout the clinical course of dementia.

6. A month later, Eric re-attends with his daughter to review his test results. The blood tests are essentially normal, but the magnetic resonance imaging scan shows 'generalized mild atrophy with sulcal widening and with evidence of white matter hyperintensity'.

- 13. Does Eric fulfil the criteria for dementia?
- 14. Should he commence a cognitive enhancing agent?
- 15. What are the current treatment considerations in terms of his practical everyday life, while ensuring his safety and legal issues?

Eric fulfils the diagnostic criteria for dementia in that he has sustained significant cognitive impairment with associated functional loss that is not better accounted for by acute or reversible conditions (see for the DSM-5 criteria of major neurocognitive disorder). The neuroimaging findings are consistent with the atrophic changes seen in AD and coexistent vascular changes, and there is no evidence of an acute or reversible pathological condition. His initial relatively high score on MMSE (25/30) may be related to his high premorbid levels of intellect, education and functioning.

Further reading **For a review of the pharmacological strategies for dementia, see:** Rodda J, Carter J. (2012) Cholinesterase inhibitors and memantine for symptomatic treatment of dementia. The British Medical Journal 344:e2986. doi:10.1136/bmj.e2986

Acetylcholinesterase inhibitors are indicated as first-line treatment in mild to moderate dementia of Alzheimer's, vascular and mixed Alzheimer's/vascular aetiology. While memantine is indicated in moderate–severe Alzheimer's, vascular and mixed Alzheimer's, it is commonly used earlier in the course of dementia as an adjunctive treatment with acetylcholinesterase inhibitors.

At this relatively early stage in his dementia, Eric should be referred to relevant agencies, such as public health, to assess his general health and functional needs. While his GP will coordinate his medical care, referral to old age psychiatry may be helpful in further clarifying the diagnosis (exact nature and severity of dementia), performing a functional assessment (through occupational therapy) and in managing behavioural and psychological symptoms of dementia (BPSD) if and when they arise (see below).

A balance should be struck between facilitating Eric's ability to live and function independently while also being mindful of his increasing and likely progressive disability and frailty. Specifically, detailed discussions should be had with Eric and his family regarding his driving; his ability to care for himself, manage his house and live independently and his plans regarding his finances, future care and legal issues such as his will and inheritance. These complex issues should be addressed as part of a sequential process. Generally, Eric should be facilitated to maintain as much of his independence, for as long as possible.

7. Eric's family are keen to meet with you to discuss his diagnosis and treatment plan. They are divided as to whether he should be present as they do not want to upset him. They are wondering about how best to plan for his future in terms of managing his personal and financial affairs.

- 16. Should Eric be present at the meeting? What are the main principles to be considered in dealing with his family?

- 17. What is an enduring power of attorney?

Giving a dementia diagnosis should be done as part of a careful process that involves Eric and his family as much as possible. While his family may have the well-meaning intention to 'protect' Eric from being given a diagnosis, he has the right to have all his questions and concerns addressed by the treating medical team. The language of such meetings can involve euphemisms such as 'memory problems' and 'thinking problems'. Technical terms, medical jargon and overly definitive statements on prognosis and life expectancy should be avoided. As a general guide, any questions of Eric's should be addressed openly and clearly, and he should not be overloaded with unsolicited information on his diagnosis, treatment and prognosis. Moreover, there may be a process involved in gradually imparting information to Eric and his family on the nature and prognosis of his dementia.

Eric and his family should also be advised that he should now arrange an enduring power of attorney (EPOA). Essentially, this involves Eric liaising with a solicitor and assigning key individuals (generally family members) to manage his financial and legal affairs if he loses the capacity to do so in future. An EPOA should be arranged as a priority once the dementia diagnosis has been clarified before his capacity is significantly diminished. If an individual with dementia loses capacity and has not already made arrangements for an EPOA, it may be required that they are made a Ward of Court, and this is a costly and cumbersome process. The Ward of Courts system is to be replaced by legislation around capacity that it

is hoped will allow for the more timely and proactive care of people with cognitive issues.

8. Nine months later, you are called at night to come and see Eric urgently. He returned home from the local hospital a week previously after a 5-day admission with a respiratory tract infection. His neighbours are concerned that he has been in the back garden in his underpants shouting for his dog 'Hugo' who has been dead for more than 10 years. When you arrive, the neighbours also tell you that he has been stopping passing traffic to enquire whether they have 'submitted an up-to-date logbook to go with their HSE mileage claims'.

- 18. What is the differential diagnosis at this point?

The immediate presentation is highly suggestive of delirium superimposed on background dementia.

The longer-term history of abnormal behaviour (stopping passing traffic) is more suggestive of BPSD. BPSD are common complications of all types of dementia, and most patients will develop one or more BPSD at some point. BPSD symptoms vary in nature and severity and include depression, agitation, wandering, aggression and psychotic symptoms.

Further reading **For a review of the best practice in managing behavioural and psychological symptoms of dementia, see:** Tible OP, Riese F, Savaskan E, von Gunten A. (2017) Best practice in the management of behavioural and psychological symptoms of dementia. Therapeutic Advances in Neurological Disorders 10(8):297–309. doi:10.1177/1756285617712979

A general approach to managing BPSD includes a clear definition of target symptoms (based on history, collateral history and mental state examination) and the ruling out of physical or modifiable factors such as delirium, pain, dehydration or constipation. Thereafter, psychiatric diagnoses should be considered, such as depression or psychosis.

Antidepressants or antipsychotic agents can be considered, along with environmental strategies (e.g. addressing routines, habits and re-orientation techniques). The use of antipsychotics is best avoided as evidence of their beneficial effects is lacking, and they are associated with an increased risk of cerebrovascular incidents when used in people with dementia. Moreover, antipsychotic agents are poorly tolerated in patients with Parkinson's disease or DLB.

F2 Schizophrenia

1. Piotr is a 45-year-old man with a longstanding diagnosis of schizophrenia. His family asks to meet with you as they are concerned that ‘although he doesn't have any strange thoughts or experiences, he has seemed chronically depressed for the past few years’. They mention that he is extremely inactive with poor self-care and hygiene, does not seem to enjoy anything and expresses little, if any, emotion. When you meet Piotr, he is dishevelled, wearing both a beanie hat and a cap despite the warm weather, with a long beard and dry skin. He has poverty of thought and speech. He attends his local day hospital every six weeks, but his key worker there tells you he does not participate in any of the scheduled activities.

- 1. What are your initial thoughts regarding this presentation?
- 2. What is this collection of symptoms called?
- 3. What is known about the management of such a constellation of symptoms?

Schizophrenia, as a syndrome, includes three constellations of symptoms that are thought to represent distinct neurobiologies:

1. Positive symptoms, which include hallucinations, delusions and disorganized thinking, speech and behaviour.

2. Negative symptoms, which include avolition (reduced drive and activity), affective blunting, alogia (reduced vocabulary), anhedonia (reduced interest and enjoyment) and asociality.

3. Neurocognitive deficits, which include inattention, impaired executive function and reduced skill acquisition.

Piotr exhibits a pattern that is suggestive of negative symptoms of schizophrenia, which include blunting of affect, avolition, lack of drive, apathy, anhedonia and alogia. In practice, it may be difficult to distinguish these symptoms from depression, which may not always present with typical biological symptoms and is common in severe and enduring mental illness (table 12).

In Piotr's case, a thorough assessment should be conducted to rule out a comorbid depressive illness and/or substance abuse. However, the longstanding nature of these symptoms suggests these are negative symptoms of schizophrenia rather than part of a depressive syndrome.

Table 12. Some Differences Between Negative Symptoms and Depression

Negative Symptoms	**Depression**
Blunted affect	Flat affect
Amotivation	Depressed mood
Anticipatory anhedonia	Anhedonia
Apathy	Guilt
Social withdrawal	Weight loss or gain
Attentional impairment	Decreased concentration
Longitudinally stable	Longitudinally unstable
Medication unresponsive	Medication responsive
Brain structural changes	Structural change less consistent
Cognitive deficits	Cognitive deficits less stable/pronounced

Negative symptoms have been observed in as many as 30% of patients with schizophrenia and in around 15% of those experiencing their first episode. These 'deficit' symptoms are thought to be related to cortical cell loss, as the illness progresses. Accordingly, there is evidence that earlier diagnosis and treatment (e.g. the duration of untreated psychosis); may impact functioning and the course of symptoms, including negative symptoms. In 15%–20% of patients with schizophrenia negative symptoms persist and have been shown to limit recovery and reduce social functioning. It is important to recognize that, while the positive symptoms of schizophrenia present a compelling therapeutic target, for the majority of patients these symptoms occur during periods of relapse and can usually be well controlled. Conversely, negative symptoms represent a much more challenging long-term therapeutic target that accounts more substantially for adaptive functioning and quality of life over time. Negative symptoms may be considered primary (inherent to the illness) or secondary to the following: (1) depression; (2) a side-effect of medication, also known as extrapyramidal symptoms (EPS; e.g. bradykinesia); (3) as a result of positive symptoms such as hallucinations/delusions, wherein a patient withdraws socially; (4) institutionalization; or (5) chronic substance misuse. Secondary symptoms should be treated by addressing the relevant cause.

Further reading **For a detailed review of negative symptoms and their management, see:** Aleman A, Lincoln TM, Bruggeman R, et al. (2017) Treatment of negative symptoms: Where do we stand, and where do we go? Schizophrenia Research 186:55–62. doi:10.1016/j.schres.2016.05.015

The pharmacological management of negative symptoms requires careful consideration of the extent to which current treatments are causing secondary

negative symptoms and the extent to which changes in treatment might impact upon primary negative symptoms in schizophrenia. The latter is a controversial issue with limited evidence that any pharmacological intervention impacts reliably upon primary negative features. A detailed meta-analysis of placebo-controlled studies demonstrated small (but not clinically significant) benefits with second-generation antipsychotics, antidepressants, combinations of pharmacological agents, glutamatergic medications and psychological interventions. As outlined below, all antipsychotics act as D_2 receptor antagonists. In addition, 5-HT2A antagonism and/or 5-HT1A agonism may contribute to the therapeutic effects of second-generation antipsychotics (SGAs). Certain SGAs have been reported to be superior to first-generation antipsychotics (FGAs) in the treatment of negative symptoms, but this effect is confounded by the observation that FGAs may cause secondary negative symptoms such as EPS. Studies of treatment with antidepressants, mainly serotonin specific reuptake inhibitors (SSRIs), have yielded inconsistent findings, with a recent detailed meta-analysis supporting the addition of an SSRI as potentially helpful. However, current treatment guidelines conclude that the evidence for augmenting antipsychotic medication with an antidepressant in the treatment of negative symptoms of schizophrenia is not currently robust enough to be recommended for clinical practice.

Further reading **For a review of nonpharmacological approaches to negative symptoms, see:** Turner DT, McGlanaghy E, Cuijpers P, et al. (2018) A meta-analysis of social skills training and related interventions for psychosis. Schizophrenia Bulletin 44(3):475–491. doi: 10.1093/schbul/sbx146

Social skills training and cognitive behavioural therapy (CBT) have demonstrated efficacy in ameliorating negative symptoms, may reduce functional impairments and enhance social competence in the areas of self-care, work, leisure and family relationships. In general, these approaches have been greatly underutilized in clinical practice until the emergence of more recovery-focused approaches, which emphasize more holistic management of mental disorders.

2. Piotr lives alone (with family members nearby) and attends a local rehabilitation day hospital. He has had numerous trials of first-generation antipsychotics over the past 20 years. Lately, he has been receiving treatment with the second-generation antipsychotics–risperidone and olanzapine. In addition to his negative symptoms, he experiences persistent beliefs that government agents are reading his mind and that he hears voices of ‘politicians commenting on everything I do’. These symptoms wax and wane and he is occasionally distressed by them.

The staff in the day hospital have noted that he has difficulties with organization and understanding the nuances of interpersonal cues and relationships.

- 4. What psychopathological condition is described here?
- 5. What is the prevalence of schizophrenia?
- 6. What are the main aetiological theories to explain the neuropathology of schizophrenia?
- 7. What do you know about the different classes of antipsychotics in terms of their side-effect profile?

Piotr is describing thought broadcasting and third-person auditory hallucinations giving a running commentary. These are both first-rank symptoms of schizophrenia. Furthermore, the day hospital staff have observed some neurocognitive deficits, including difficulties with executive functioning, such as the ability to organize and abstract.

It is well recognized that patients with schizophrenia have significant neurocognitive deficits when compared with the normal population. These include difficulties with verbal and working memory, attention and concentration, executive functioning and processing speed. These difficulties impact upon the level of autonomy in patients with schizophrenia in terms of self-care, vocational outcomes, family contact and social functioning.

Causes of schizophrenia. There are several aetiological theories for schizophrenia, all falling under the umbrella of the neurodevelopmental hypothesis. A higher rate of motor and cognitive problems is evident for years before the more florid symptoms of acute illness. The neurodevelopmental theory relates to the typical onset of florid symptoms during the time of dopamine receptor 'pruning'. Epidemiologically, it has been noted that those born after obstetric complications, in winter or early spring are at greater risk of the illness. Overactivation of the immune system from prenatal infection or postnatal stress may result in the overexpression of inflammatory cytokines and subsequent alterations in brain structure and function. There is also a clear genetic component. The lifetime risk of schizophrenia in the general population is just below 1%, rises to 6.5% in the first-degree relatives of affected individuals and is higher than 40% in those with an affected monozygotic twin.

The dopamine hypothesis. The development and effectiveness of haloperidol (a first-generation antipsychotic of the butyrophenone family) in the 1950s led to the emergence of the dopamine hypothesis as the central

neurobiological underpinning of schizophrenia. According to the dopamine hypothesis, central dopaminergic hyperactivity in the mesolimbic tract precipitates positive symptoms, while the disrupted dopamine activity in the mesocortical circuits may explain the negative symptomatology.

Haloperidol, along with other antipsychotics, act as D2 receptor antagonists, with various degrees of affinity to the receptor. In addition, 5-HT2A antagonism and/or 5-HT1A agonism may contribute to the therapeutic effects of the SGAs. These receptors in the prefrontal cortex are also thought to contribute to the pathology of the negative symptoms. Other dopamine tracts are implicated in the development of side-effects (table 13).

Table 13. Dopamine Tracts

Dopamine Tract	Function	Dopamine Antagonist Effect
Nigrostriatal	Extrapyramidal system, movement	Movement disorders (acute dystonia, akathisia, parkinsonism and tardive dyskinesia)
Mesolimbic	Emotional functioning, motivational behaviour	Relief of psychosis
Mesocortical	Cognition, executive function	Relief of psychosis, akathisia, worsening of negative symptoms
Tuberoinfundibular	Regulates prolactin release	Hyperprolactinaemia

First-generation antipsychotics. FGAs all act by dopamine antagonism. In general, high potency antipsychotics (e.g. haloperidol, fluphenazine) cause greater EPS than low potency agents (e.g. chlorpromazine, thioridazine). In contrast, low potency agents cause more sedation and anticholinergic side-effects. In addition, these agents can cause significant prolongation of the QT interval on electrocardiogram, which can precipitate a ventricular arrhythmia called ‘torsades de pointes’.

Second-generation antipsychotics. SGAs have a rapid dissociation at D2 receptors and a strong affinity for blocking 5-HT2A receptors, therefore demonstrating a sustained antipsychotic effect with a significantly lower risk of EPS. Moreover, they have been associated with improved compliance. They have multiple additional receptor binding affinities and some of their adverse effects can be explained by their action at histaminergic, cholinergic, alpha-adrenergic receptor blockade. SGAs are also associated with a variety of side-effects. Olanzapine, clozapine and quetiapine are particularly associated with sedation. Clozapine and olanzapine have well recognized anticholinergic effects and are

especially associated with adverse metabolic effects, including weight gain, hyperglycaemia and dyslipidaemia that have been the subject of litigation in the United States. It is recommended that those patients who are prescribed an atypical drug associated with weight gain, and especially those with cardiovascular disease, have regular metabolic monitoring that includes weight, glycaemic status and lipids measured regularly. Risperidone and amisulpride are implicated in hyperprolactinaemia and can cause unwanted side-effects of gynecomastia, galactorrhoea, abnormalities of the menstrual cycle, impotence and osteoporosis. SGAs are also associated with QT prolongation .

Clozapine is currently licensed for treatment-resistant schizophrenia, which is defined by the lack of response to adequate trials of two or more conventional antipsychotics (one of which must be an SGA). Clozapine was first used in the 1960s but was withdrawn from the market following recognition of its association with neutropenia and agranulocytosis. Around 2%–3% of patients treated with clozapine will develop neutropenia, and less than 1% will develop agranulocytosis. In many countries, the re-introduction of clozapine was supported by regular full blood count monitoring with emphasis upon the potential for neutropenia. This typically involves a weekly blood test that can be stretched to fortnightly and monthly testing over time as agranulocytosis becomes less likely with sustained use. Later, in 1988, it was shown that clozapine was more effective than conventional antipsychotics, and it was dispensed in the United Kingdom, although with compulsory monitoring for neutropenia and agranulocytosis.

Further reading **For a review of the effectiveness of antipsychotic agents, including clozapine, see:** Siskind D, McCartney L, Goldschlager R, Kisely S. (2016) Clozapine v. first- and second-generation antipsychotics in treatment-refractory schizophrenia: systematic review and meta-analysis. British Journal of Psychiatry 209(5):385–392. doi:10.1192/bjp.bp.115.177261

Clozapine remains the only antipsychotic known to be efficacious in individuals with treatment-resistance and has superior efficacy in decreasing suicidal behaviour and violence. Clozapine is a powerful drug in treatment-resistant illness. As a general rule patients who have failed two previous antipsychotic medication trials experience full symptom remission (one-third), partial symptom remission (one-third) and minimal response (one-third). Clozapine has a complex pharmacodynamic profile with multiple receptor actions that also bring a variety of adverse effects, such as sialorrhea (excessive salivation), sedation, weight gain, metabolic disturbance and seizures.

In Piotr's case, it would be appropriate to discuss a trial of clozapine at this point while raising the practical aspects of its prescription, including regular monitoring of his full blood count, the importance of adherence and other potential side-effects.

The risk of myocarditis (<1%) and lowering of seizure threshold should be discussed along with the likelihood of weight gain, hypersalivation and sedation. The pharmacology of clozapine differs substantially from other antipsychotics in that it binds weakly to D_1 and D_2 receptors. However, it has an affinity for D_4, $5HT_2$, $5HT_3$, α_1 and α_2 adrenergic, ACh M_1, and H_1 receptors. It has not been established which individual or combination of these receptors is responsible for the efficacy of clozapine. Clozapine is associated with an extremely low rate of EPS and it is not believed to cause tardive dyskinesia.

3. Despite your encouragement, Piotr is reluctant to take clozapine, as he is not keen on the idea of regular blood testing and states that ‘none of your tablets ever seem to make any difference’. You note that he has longstanding orofacial grimacing and that his feet seem to be moving without his voluntary control. He is disorganized, with a blunted affect, and he appears more distressed by his systemized delusions that the government is monitoring him. There is no evidence of suicidal or homicidal thinking. Piotr clearly states that he is not prepared to make any further changes to his medications and no longer wishes to attend the day hospital. He agrees to see you on a six-monthly basis only. His family remain concerned and ask for a ‘brain scan… in case you have misdiagnosed him’. Staff at the day hospital report that Piotr is smoking more heavily than normal, and he has been seen in the company of other service users who have had issues with substance misuse.

- 8. What do you think these motor symptoms are and what do you understand about the mechanism of their development?
- 9. How are they treated?
- 10. How would you address possible substance misuse?
- 11. What is known about the radiological findings in schizophrenia?

EPS include dystonia (continuous spasms and muscle contractions), akathisia (motor restlessness), parkinsonism (characteristic symptoms such as rigidity), bradykinesia (slowness of movement), tremor and tardive dyskinesia (irregular, jerky movements). These features differ in their timing with dystonic reactions typically occurring within hours of commencing an antipsychotic, parkinsonism within days or weeks, acute akathisia within hours to weeks and

tardive dyskinesia, usually only after many months or years of treatment. In parkinsonism, bradykinesia can be easily mistaken for either depression or negative symptoms of schizophrenia. Physical examination should aid in its identification as it is frequently accompanied by rigidity in parkinsonism.

Further reading **For a review of combination treatment strategies in schizophrenia, see:** Correll CU, Rubio JM, Inczedy-Farkas G, et al. (2017) Efficacy of 42 pharmacologic cotreatment strategies added to antipsychotic monotherapy in schizophrenia. JAMA Psychiatry 74(7):675–684. doi:10.1001/jamapsychiatry.2017.0624

Piotr appears to have tardive dyskinesia, which is caused by the super-sensitivity of dopamine receptors in the nigrostriatal pathway. Briefly, there should be a withdrawal of any prescribed anticholinergic agent, lowering of the dose of an antipsychotic agent (which may temporarily worsen the dyskinesia) and consideration of substitution with a less 'potent' agent. In this case, clozapine is the most appropriate medication.

In terms of treatment-resistance if, as is the case with Piotr, clozapine is not a preferred option, combinations of antipsychotic agents are often used in clinical practice to broaden receptor binding affinity. However it should be noted that there is a limited evidence base for this approach.

Further reading **For a review of family interventions in schizophrenia, see:** Pharoah F, Mari J, Rathbone J, Wong W. (2010) Family intervention for schizophrenia. Cochrane Database of Systematic Reviews 12:CD000088. doi:10.1002/14651858.CD000088.pub2

At this point it would be prudent to reassess Piotr's diagnosis, rule out any comorbid substance abuse and assess any current stressors, such as 'expressed emotion (EE)' in the home. People with schizophrenia from families that express high levels of criticism, hostility or over-involvement (i.e. high EE), have more frequent relapses than people with similar problems from families that tend to be less expressive of emotions. There is consistent evidence that high EE (including controlling attitudes, hostility and criticism) has discernible pathophysiological effects and a significant correlation with relapse frequency. Typical interventions include reducing exposure to the high EE environment (e.g. with daytime placements in day facilities). There is some evidence that family-based psychoeducational interventions can reduce the level of EE and that this is associated with better medication compliance, fewer relapses and fewer periods of hospitalization.

Drug analysis. Substance misuse is common in individuals with schizophrenia. Although there is a marked variation between studies, as many as 50% of affected individuals abuse alcohol or other substances. In addition, around 70% are addicted to nicotine. Cigarette smoking appears to regulate the mesolimbic dopamine system and improves cognitive performance by reducing so-called 'hypofrontality'. As such, it may be a form of self-medication. Conversely, it is a postulated causal factor in the development of psychosis and may significantly decrease antipsychotic levels (clozapine).

Further reading **For a review of testing for illicit drug use in mental health services, see:** Abraham A, Luty J. (2010) Testing for illicit drug use in mental health services. Advances in Psychiatric Treatment 16(5):369–379. doi:10.1192/apt.bp.108.005835

As in Piotr's case, when there is an inconsistency between history (there are no clear precipitating causes for his deterioration) and clinical symptoms/signs, drug testing may be necessary. On-the-spot screening by urine testing is usually sufficient. Nonetheless, confirmatory laboratory tests may be indicated if there is a diagnostic dilemma, if the patient disputes a screening result, or if there are serious implications to a positive result (e.g. in child protection cases). Urine screening is inexpensive and simple to administer with instant results. However, its usefulness may be limited by adulteration, urine tampering and false-positives. A further complication is that long-term cannabis use can produce positive results in the urine up to 45 days after cessation.

Neuroimaging is indicated as part of the workup in individuals presenting with a first psychotic episode and may be considered in those with an established psychotic illness for whom their symptomatology changes dramatically. In both situations, the primary role of neuroimaging is to rule out organic factors such as an intracerebral tumour or stroke. Despite the request, there is no diagnostic test for the presence of schizophrenia. However, there is an increasing body of research identifying the neurobiological underpinnings associated with psychotic illnesses. Structural magnetic resonance imaging findings in patients with schizophrenia have revealed widespread reductions in grey matter (GM). GM reduction in the medial temporal lobe structures, thalamus, basal ganglia, amygdala, hippocampus, parahippocampal gyrus and neocortical temporal lobe regions is linked to lateral ventricular enlargement and third ventricle enlargement.

Further reading **For a review of the findings from functional image studies in schizophrenia, see:** Fitzsimmons J, Kubicki M, Shenton ME. (2013)

Review of functional and anatomical brain connectivity findings in schizophrenia. Current Opinion in Psychiatry 26(2):172–187. doi:10.1097/YCO.0b013e32835d9e6a

Studies have investigated the disordered functional brain anatomy of both the positive and negative symptoms of schizophrenia. These indicate that hallucinations are associated with abnormal brain activity in primary and secondary sensory areas. Disordered activation in nonsensory regions appears to contribute to the emotional impact of hallucinations as a factor underlying an inability to distinguish ongoing mental processing from memories. Brain activation studies support the view that auditory or verbal hallucinations are associated with an impaired ability of internal speech plans to modulate neural activation in sensory language areas. Negative symptoms of schizophrenia are associated with impaired function in frontal brain areas with resting blood flow and metabolism in the frontal cortex reduced in schizophrenia. Brain activation studies indicate impairment of working memory functioning and are linked to impaired functional connections between the frontal and temporal cortex.

4. Piotr's family meet with you to discuss further management options. They are concerned that his condition will deteriorate without more regular contact with the services. After meeting with the mental health advocacy services, they understand the limitations of medication and are interested in other models of care. They are particularly interested in the possibility of CBT. The meeting with the advocacy service has made them more optimistic in general, especially as the advocate told them that all service users could ‘recover’ from mental illness.

- 12. What nonpharmacological treatment options are available for the management of schizophrenia?
- 13. What is the prognosis in severe and enduring mental illness?
- 14. How would you respond to the family's observation about ‘recovery?’

Psycho-social interventions. There are a variety of augmented models of routine care that may help to alleviate symptoms of chronic illness, improve engagement with services and improve social and occupational dysfunction. These interventions work in synergy with pharmacological approaches and are traditionally provided by rehabilitation and recovery teams in the Irish setting.

Prognosis. The prognosis for individuals with schizophrenia varies considerably. Overall, the life expectancy of persons with severe and enduring mental illness (e.g. schizophrenia) is 12–15 years shorter than for the general

population. This effect is principally mediated by lifestyle issues and reflected in cardiovascular disease, respiratory illnesses and cancer statistics. In addition, the lifetime risk of suicide is significantly raised at 5%–10%. The historical observation that one-third of affected individuals recover, one-third remit/relapse and one-third deteriorate appears to under-represent those with a favourable prognosis as demonstrated in more recent studies. The course of the first two years appears to predict long-term outcomes. Therefore, perhaps logically early intervention at medical, social and psychological levels is associated with long-term benefits.

Recovery. Response to intervention in schizophrenia is often referred to in terms of remission and recovery. For 'remission' the Diagnostic and Statistical Manual of Mental Disorders requires that there should be a 'complete return to full functioning', while other definitions require specific symptoms to be controlled and not interfering with functioning. Further complexity has risen with service user-defined concepts of recovery. The 'recovery model' (which the mental health advocate in this case has referred to) incorporates a wide range of factors, which may be at odds with clinician defined criteria. The model has been described as a 'journey' (analogous with the recovery of those with addictions), that emphasizes user-empowerment, hope and optimism, personal responsibility, autonomy, self-management and person-centred treatments. The recovery model focuses on collaborative treatment approaches, finding productive roles for users, peer support and reducing stigma. The model is viewed by many as an antidote to the lack of optimism that many perceive with the medical model, which has significant limitations in terms of effectiveness for many people with a severe and enduring illness. The recovery approach is increasingly incorporated into the development of mental health services around the globe.

Further reading **For a discussion of the recovery model in schizophrenia, see:** Warner R. (2009) Recovery from schizophrenia and the recovery model. Current Opinion in Psychiatry 22(4):374–380. doi:10.1097/YCO.0b013e32832c920b

The recovery approach considers 'illness' and 'wellness' as independent variables and services have increasingly incorporated these values. It is apparent that, although schizophrenia remains a serious illness with a higher morbidity and mortality, most individuals with the condition can live a meaningful and satisfying life in the presence of treatment-resistant symptoms.

F3 Bipolar disorder

1. Caroline is a 31-year-old supermarket manager who has been attending mental health services for almost 10 years and has an established diagnosis of bipolar I disorder. She has previously experienced several episodes of illness and undergone three previous hospitalizations with acute mania (twice) and depression (once). Her illness has been stable for the past five years since commencing lithium therapy. She is attending for a routine three-monthly review.

- 1. What is the significance of the diagnosis of bipolar I disorder?
- 2. What is lithium and what is the evidence for its use in bipolar illness?
- 3. What is the proposed mechanism of action for lithium?

Bipolar I disorder is characterized by a clinical course that includes the occurrence of one or more manic or mixed episodes (i.e. episodes with features of low mood/irritability with elation). Usually, individuals have also had one or more major depressive episodes such that a pattern of unipolar mania is unusual, especially over longer-term follow-up. Episodes of substance-induced mood disorder (because of the direct effects of a medication, or other somatic treatments for depression, a drug of abuse or toxin exposure) or of mood disorder due to a general medical condition do not count toward a diagnosis of bipolar I disorder. In addition, the episodes are not better accounted for by schizoaffective disorder and are not superimposed on schizophrenia, schizophreniform disorder or a psychotic disorder not otherwise specified. In contrast, the essential feature of bipolar II disorder is a clinical course that is characterized by the occurrence of one or more episodes of major depression accompanied by at least one hypomanic episode. Hypomania is less severe than mania in terms of its impact upon socioadaptive functioning, and does not include overt psychosis. Episodes of substance-induced mood disorder (because of the direct effects of a medication, or other somatic treatments for depression, a drug of abuse or toxin exposure) or of mood disorder due to a general medical condition can count toward a diagnosis of bipolar II disorder. A further consideration is that of cyclothymia, which is chronic mood disorder widely considered to be a more chronic but milder or subthreshold form of bipolar affective disorder. It occurs in 1% of the population, but recognition rates are increasing. Cyclothymia is characterized by numerous mood swings that typically last days or weeks that involve periods of elevated mood and increased activity that do not meet the criteria for a manic episode, alternating with periods of mild or moderate symptoms of depression that do not meet the criteria for a major depressive episode. Such persons are often considered ‘moody’ by friends

and family. This can represent a prodromal phase for full bipolar illness. Although the emotional highs and lows of cyclothymia are less extreme than those of bipolar affective disorder, the symptomatology, longitudinal course, family history and treatment response of cyclothymia are consistent with bipolar spectrum. Importantly, the frequency of bipolar illness is elevated in those with cyclothymia, and twin studies indicate high concordance in monozygotic twins.

Comparison of bipolar I and bipolar II disorder. Dividing bipolar illness into I and II has an obvious phenomenological basis, but there are pathophysiological, therapeutic and prognostic differences as well. A detailed longitudinal study of the course of bipolar illness over 20 years found the following:

- Bipolar I and II patients had similar demographics and ages of onset at the first episode.
- Bipolar I patients had more severe acute episodes.
- Both had more lifetime co-occurring substance abuse than the general population.
- Bipolar II had significantly higher lifetime prevalence of anxiety disorders, especially social and other phobias.
- Bipolar II patients experience a substantially more chronic course, with significantly more depressive episodes with shorter periods of remission between episodes.

From a genetic perspective, concordance between monozygotic twins for bipolar I disorder is 30%–90%. Other work indicates that the risk of bipolar II disorder is elevated in both bipolar I and II patients, but that the risk of bipolar I does not appear to be markedly increased in the relatives of those with bipolar II disorder.

A variety of studies have identified genetic variants that predict lithium responsiveness (Rev-erb-Alpha, BDNF and Glycogen Synthase Kinase 3-Beta). Lithium is a mood-stabilizing agent that is generally considered to be the first-line treatment for the prophylaxis of classical bipolar illness. Its use has been well studied, compared to other mood stabilizers, and is supported by multiple placebo-controlled trials that have indicated a significant preventative action versus illness relapse. It is less effective in atypical illness, such as that which involves mixed affective presentations or rapid cycling. Lithium can also be used in the management of acute mania, but has a delayed onset of action and modest sedative

properties, and typically requires augmentation with other agents. Although lithium has been in use for over 50 years and has well-established effectiveness, its mechanism of action is not well understood. Lithium is a basic element that can substitute for sodium, potassium, calcium or magnesium in cellular systems and influences neurotransmitter release, receptor upregulation and activation of second messenger systems. It has been postulated that these effects act to stabilize cell membranes, and that this is the mechanism of action in bipolar illness wherein destabilized neurotransmission and/or kindling are suggested pathophysiologies. Of note, 'kindling' in neurobiology refers to a process whereby the occurrence of an event sensitizes the brain to further similar events at a higher intensity. It is applied to epilepsy in terms of the notion that 'seizures beget more seizures'. In terms of mood disorder, it may apply in terms of having an increasing propensity for episodes as more episodes occur. Interestingly, lithium contrasts with most psychoactive agents in that it typically produces no obvious psychotropic effects in normal individuals at therapeutic concentrations.

***Suggested mechanisms for the mood-stabilizing effect of lithium*:**

• Decreasing norepinephrine release

• Increasing serotonin synthesis

• Modulating N-methyl-D-aspartate (NMDA) receptor/nitric oxide signalling

• Neuroprotective properties acting against oxidative stress by upregulating complex I and II of the mitochondrial electron transport chain

• Altered dopamine-associated G-protein function

• Lithium competes with magnesium for binding to NMDA glutamate receptor, increasing the availability of glutamate in postsynaptic neurons

• Lithium has mixed effects on cyclic adenosine monophosphate (cAMP): it increases basal levels of cAMP but also impairs receptor coupled stimulation of cAMP production

• Effects on inositol-phosphate activity: lithium inhibits the enzyme, inositol monophosphatase, which is involved in degrading inositol monophosphate to inositol.

2. At review, Caroline reports a recent worsening of her mood, especially in the morning, and that she has been feeling low for most of the day. This has also been associated with sluggishness and a general lack of interest in things. She is wondering if this is related to her lithium treatment.

• 4. What are the possible causes of this presentation and how can they be further explored?

- 5. What are the problems that can occur with lithium therapy and how should they be monitored for?

While the occurrence of depressive illness is always a key consideration in patients with affective disorder, especially when there is evidence of lowering of mood and altered functioning of biological functions, it is also important to be aware that normal sadness or fatigue, secondary to everyday life events, occur in everyone and are not necessarily indicative of a morbid process. In addition to usual medical causes of low energy (e.g. anaemia, hypothyroidism, diabetes, chronic obstructive pulmonary disease, sleep apnoea, chronic infection, post-viral illness), the potential role of treatment effects should be considered (e.g. sedation). Hypothyroidism secondary to lithium use is common (occurring in up to one-third of users and more common in females). This is readily diagnosed and can usually be treated with thyroxine without discontinuation of lithium. The differential diagnosis includes a depressive episode, a physical illness that is not directly related to the bipolar diagnosis or its treatment, sedative or other adverse effects of treatment (e.g. hypothyroidism) and normal sadness. Distinguishing these causes is achieved by taking a thorough history exploring the context of these difficulties in terms of onset and progression and relationship to life events and treatment exposures, ascertaining the presence of cognitive and somatic symptoms of depression, other physical symptoms that might indicate an organic cause (e.g. thinning of hair, hypersomnia, fatigue, increased sensitivity to cold, constipation, weight gain, muscle weakness) and physically examining for anaemia, goitre and bradycardia. The usual comprehensive battery of tests for fatigue, including thyroid function tests, are also indicated. This presentation can be investigated by taking a thorough history for symptoms of clinical depression, symptoms indicative of hypothyroidism, recent physical illness and medication/drug exposure. The nature and severity of low mood and its relationship to other symptoms, such as fatigue, are important to clarify. Usual blood screening [full blood count (FBC), urea and electrolytes (U&E), liver function tests (LFT)], lithium levels and thyroid function tests, are essential tests that should be performed initially.

Prescribed substances that can cause elation:

- Steroids: Cortico and anabolic compounds
- Stimulants, e.g. methylphenidate, D-amphetamine, fenfluramine
- Antidepressants [especially tricyclic antidepressants and serotonin and noradrenaline reuptake inhibitors (SNRIs)]

Lithium therapy is well tolerated by many patients, but 75% will experience some adverse effects, and typically 50% of users discontinue use within 12–24 months of initiation. Problems with lithium therapy can be broadly separated into effects caused by acute toxicity and effects that occur over time with sustained use.

Lithium toxicity is typically an acute syndrome caused by elevated serum lithium levels because of accidental or deliberate overdose, interactions with drugs that promote raised serum levels (especially diuretics, nonsteroidal antiinflammatory drugs, calcium channel blockers), severe dehydration because of vomiting, diarrhoea, heatstroke, or accumulation because of reduced renal excretion. Prophylactic serum levels are between 0.6 and 1.2 mmol/L. Toxicity typically appears at levels of ≥1.5 mmol/L with headache, nausea and other gastrointestinal upset progressing to tremor, blurred vision, ataxia, impaired consciousness, seizures, cardiac arrhythmias, coma as levels increase. It represents an acute medical emergency.

Lithium use is also associated with a variety of possible adverse effects:

- 1. Hypothyroidism
- 2. Impaired renal function (typically after sustained use over many years) and that is usually reversible (irreversible in approx. 1% of users)
- 3. Weight gain and oedema because of fluid retention
- 4. Polyuria and polydipsia
- 5. Gastrointestinal upset
- 6. Sedation and/or lethargy
- 7. Tremor
- 8. Benign leucocytosis
- 9. Cardiac conduction problems (usually benign T-wave changes and prolonged QRS)
- 10. Teratogenesis.

Lithium monitoring guidelines (Maudsley guidelines):

It is recommended that lithium levels be monitored weekly until stable serum levels are achieved to minimize the potential for side-effects. Thereafter, for most patients (i.e. those without specific issues):

- Lithium levels should be measured every three months.
- Thyroid function, U&E, FBC and LFT should be checked every six months.
- Creatinine clearance and an electrocardiogram should be measured annually.

Lithium levels are measured 12 hours after the last dose, which is usually in the early to mid-morning, as lithium is usually taken before going to bed because of its mild sedative effects. It is important to clarify when the last dose was taken as lithium has a short half-life such that for patients who usually take lithium in the morning, this can artificially elevate levels. Conversely, some patients may erroneously discontinue lithium for a period prior to testing of serum levels. The glomerular filtration rate (GFR) is a key indicator of renal function. The estimated GFR provides a useful measure of renal function that is relevant to lithium-related change. The eGFR is a mathematically derived entity based on a patient's serum creatinine level, age, sex and race. A normal level is 90 mL/min. Five levels of impaired renal function are noted and can be classified according to eGFR. Levels between 60 and 90 mL/min reflect stage 1 and 2 chronic kidney disease (CKD), which can be consistent with normal ageing. Below 60 mL/min is more concerning (stage 3–5 CKD), but importantly, the longitudinal trend of eGFR is crucial to make decisions over lithium use such that a stable value below this can be acceptable. In contrast, a declining value requires careful consideration of the need to explore lithium discontinuation.

3. Caroline also reports weight gain, fatigue, hypersomnia, thinning of her hair and that she has been feeling cold all the time. Investigation reveals that her lithium levels are 0.7 mmol/L and that her thyroid-stimulating hormone levels are significantly elevated with reduced T4 levels. After discussion, she agrees to continue lithium and commence L-Thyroxine along with escitalopram (a serotonin specific reuptake inhibitor; 10 mg per day). However, over the coming weeks, her low mood worsens despite increasing her escitalopram dose to 20 mg per day. After eight weeks, she commences venlafaxine (a serotonin and noradrenaline reuptake inhibitor; 225 mg), which improves her mood.

- 6. What is the therapeutic range for lithium levels?
- 7. How does the treatment of bipolar depression differ from that occurring in unipolar illness?
- 8. What features of a depressive episode suggest that it is more likely to be part of a bipolar than unipolar illness?

The therapeutic range for lithium is widely accepted to be between 0.4 mmol/L and 1.2 mmol/L. Some evidence suggests that patients who are maintained above 0.6 mmol/L have a lower rate of relapse than those who are maintained between 0.4 and 0.6 mmol/L. Moreover, most psychiatrists aim for levels between 0.6 and 1.0 mmol/L. The distinction between unipolar and bipolar affective disorder is important for many reasons. These include managing the likelihood of

the so-called ‘switching’, whereby antidepressant interventions can precipitate hypomanic or manic episodes, and in identifying optimal treatment for depressive episodes. Depressive episodes occurring in patients with bipolar affective disorder are often more challenging to manage as they are less likely to respond to conventional antidepressants [e.g. serotonin specific reuptake inhibitors (SSRIs)]. In contrast, treatment with more potent antidepressants (e.g. tricyclic agents or SNRIs) is associated with a risk of precipitating (hypo)mania and in extreme cases destabilizing the underlying illness, with the emergence of rapid cycling illness (see below). Furthermore, in patients with suspected bipolar illness, the approach to managing depressive episodes includes optimizing mood stabilizer therapy, being aware that usual antidepressant interventions may be less efficacious and having an open mind about the value of using alternative strategies, such as other antidepressant classes, another mood stabilizer or antipsychotic augmentation strategies. Many clinicians believe that unopposed antidepressant therapy (i.e. without a concomitant mood stabilizer or antipsychotic) should be avoided.

The National Institute for Health and Care Excellence guidelines recommend that bipolar depression is initially treated with an SSRI as first-line therapy and that second-line approaches include either: (i) switching to mirtazapine or venlafaxine or (ii) augmentation with mirtazapine, quetiapine, olanzapine or lithium.

The diagnosis of bipolar illness is often delayed, particularly in patients who present with depressive episodes without evidence of periods of elation. Of note, in many cases, there are episodes of elation. However, these can be overlooked unless specifically explored for (enquire about the following: sustained periods of unusually high levels of energy, reduced sleep requirement, elevated confidence and/or disinhibition with spending, hypersexuality or other risk-taking behaviours). In addition, there are clues in the presentation of depression that suggest a higher likelihood that the actual diagnosis is a bipolar illness. These include a positive family history of bipolar illness; early age of onset; severe episodes, including any with psychosis; relative treatment resistance (e.g. to SSRIs); and presence of atypical features, such as hypersomnia, increased appetite or mixed features. In such cases, it can be useful to manage patients with the likelihood of bipolarity in mind and, therefore, emphasize mood-stabilizing interventions in treatment.

4. Ten days later, Caroline is referred for an urgent review. Her mother reports that she has not been sleeping well, is overtalkative and has been purchasing large amounts of expensive lingerie online. Her workmates have

expressed concern that she has been inappropriate and overfamiliar with customers, offering substantial price reductions for goods. She reports feeling ‘fundamentally liberated’ but also upon discussion accepts that she may perhaps be ‘a little high’. She does not report any ideas that might be delusional in intensity and denies other psychotic phenomena. She is not keen to be admitted to hospital and her mother volunteers to ‘keep an eye on her for a few days’.

- 9. What is your diagnosis and immediate management plan?

These disturbances suggest that Caroline is experiencing an episode of hypomania rather than full mania as she has been able to continue her usual day-to-day routine and does not have evidence of any psychotic symptoms. Her relative insight into the probable nature of her recent behaviour also suggests hypomania, especially given her willingness to take appropriate treatment along with the availability of continuous and well-informed support. It appears reasonable to proceed with community-based treatment, albeit with regular review of her progress in case her circumstances deteriorate. It is important with bipolar illness to recognize the longer-term picture and to develop a collaborative relationship as this means that help-seeking is likely to be earlier, which can prevent full-blown episodes. Moreover, a key principle of mental health legislation is that treatment should always be provided in the least restrictive environment that is possible, available and rational in terms of perceived risks. Equally, it is important to try to prevent unnecessary loss of social capital. The statistics regarding a substantially elevated risk in patients with bipolar disorder in terms of experiences relating to the loss of employment, financial difficulties and experience of marital failure emphasize the need to minimize exposure to socially damaging situations. This is a balance that requires careful consideration in collaboration with the patient and is frequently enhanced by having good collateral sources of information about the extent of any behavioural changes that are evident. It can be useful to explore preferences for how a ‘high’ should be managed with the patient when they are stable and normothymic.

5. You agree to manage Caroline's symptoms as an outpatient, and she agrees to commence risperidone (3 mg nocte). Her mental state settles over the following week. At the review, it emerges that she decided not to take the serotonin and noradrenaline reuptake inhibitor as prescribed. There are no other obvious explanations for the deterioration in mental state. She is worried that the ‘lithium may have stopped working’ and wishes to discuss the pros and cons of alternative approaches to the prevention of episodes. Moreover, she is interested in

exploring the implications of lithium for pregnancy as she has been in a stable relationship for three years and has been thinking about settling down and starting a family.

- 10. What are the alternatives to lithium for maintenance treatment of bipolar affective disorder?
- 11. What are the implications of lithium for pregnancy and childbirth?
- 12. What are the implications of discontinuing lithium treatment?

Lithium is the prototype for a class of agents frequently referred to as mood stabilizers. In essence, these are medications that can treat both mania and depression, although the evidence that many of these agents treat both poles of bipolar illness is quite limited and the definition is often extended to include agents that treat either depression or mania and rarely cause the other pole to become worse in the process. Lithium is generally considered the most effective mood-stabilizing agent and, in reality, most mood stabilizers are primarily antimanic agents that also impact upon, mood cycling and shifting, but are not effective at treating acute depression. Lithium, quetiapine and lamotrigine are the principal exceptions with evidence that they are effective in treating both manic and depressive symptoms. A recent detailed systematic review of randomized controlled trials of bipolar maintenance treatment (Severus et al., 2014) highlighted that lithium is more effective than a placebo in preventing overall mood episodes, manic episodes and depressive episodes. Lithium was superior to anticonvulsants in the prevention of manic episodes.

Further reading **For a review of maintenance management of bipolar affective disorder, see:**Severus E, Taylor MJ, Sauer C, et al. (2014) Lithium for prevention of mood episodes in bipolar disorders: systematic review and meta-analysis. International Journal of Bipolar Disorders 2(1):15. doi:10.1186/s40345-014-0015-8

Valproate is the agent that is typically used as an alternative to lithium. Interestingly, despite the evidence to favour lithium as a first-line treatment, in the United States and Australia, valproate is the preferred agent perhaps because of concerns about the adverse effects of lithium and/or the need for relatively less intense monitoring. Furthermore, valproate is considered to be more effective in treating ‘mixed state’ symptoms and rapid cycling. Alternatively, valproate is often used as a second-choice mood stabilizer. In support of its use, a recent study by Geddes and colleagues (2010) found that lithium or the combination of lithium and

valproate was superior to valproate alone in preventing relapse in patients with bipolar I disorder.

Further reading **For details of a recent study on relapse prevention in bipolar I disorder, see:** Geddes JR, Goodwin GM, Rendell J, et al. (2010) Lithium plus valproate combination therapy versus monotherapy for relapse prevention in bipolar I disorder (BALANCE): a randomised open-label trial. The Lancet 375(9712):385–395. doi:10.1016/S0140-6736(09)61828-6

In addition, a variety of other anticonvulsants are used in the maintenance treatment of bipolar illness with variable effect. However, there is limited evidence for their efficacy. Carbamazepine is frequently used in those who do not respond to lithium and/or valproate in the management of acute mania and mixed affective episodes. Lamotrigine is typically used for bipolar depression while there is minimal evidence for oxcarbazepine, gabapentin and topiramate. In recent years there has been a movement to formally recognize antipsychotic agents as potential mood-stabilizing agents because of evidence that quetiapine, olanzapine, risperidone and aripiprazole are effective for managing mania but may also improve bipolar depression. This practice is an extension of the longstanding empirical use of antipsychotics beyond the acute phase at low dose in bipolar patients, including sometimes by intramuscular depot formulations.

Further reading **For a discussion on issues relating to lithium use in pregnancy and cardiac malformations, see:** Patorno E, Huybrechts KF, Bateman BT, et al. (2017) Lithium use in pregnancy and the risk of cardiac malformations. New England Journal of Medicine 376(23):2245–2254. doi:10.1056/NEJMoa1612222

Lithium has well-established teratogenic potential and use in women of childbearing age requires careful consideration of the relative risk–benefit ratio. Lithium exposure during the first trimester of pregnancy is associated with a congenital heart defect called Ebstein's anomaly (a tricuspid valve abnormality) in approximately 1/600–1/1000 cases. However, there are considerable risks associated with discontinuing lithium with relapse rates in lithium responders estimated to be as high as 30% within a month of rapid discontinuation. Even with gradual discontinuation, there is an estimated three-fold greater risk of relapse within a year. Moreover, targeted discontinuation and reinstatement after the first trimester are unrealistic, and for many patients, the continuation of lithium is preferable to discontinuation. Similarly, valproate is associated with a variety of major and minor malformations. These include a 20-fold increase in neural tube

defects, cleft lip and palate, cardiovascular abnormalities, genitourinary defects, developmental delay, endocrinological disorders, limb defects and autism. Additionally, it should be avoided in women who are at risk of becoming pregnant. Carbamazepine is also linked with an elevated risk of neural tube defects, but this is thought to be less than that associated with valproate.

6. Over the following six months, Caroline experiences an unstable period alternating between periods of low mood, including an admission with mania. Her mother asks to see you to discuss what is happening. She is concerned about a reference to 'rapid cycling' that she came across on the internet. She also informs you that she suspects that Caroline has not been taking her medication regularly and has discovered a store of unused lithium.

- 13. What is 'rapid cycling' and what implication does it have for treatment?
- 14. What can be done to address problems with poor adherence?
- 15. What are your thoughts about the store of unused lithium?

Further reading **For a review of rapid cycling in bipolar affective disorder, see:** Carvalho AF, Dimellis D, Gonda X, et al. (2014) Rapid cycling in bipolar disorder: a systematic review. Journal of Clinical Psychiatry 75(6):e578–586. doi:10.4088/JCP.13r08905

Rapid cycling is a pattern of frequent, distinct episodes in bipolar affective disorder. In rapid cycling, a person with the disorder experiences four or more episodes of mania or depression in one year. Rapid cycling is not a diagnosis or a distinct subtype of the illness but rather a 'course specifier' or descriptor of a more aggressive phasic course of illness. It can occur at any point in the course of bipolar affective disorder and runs a variable and transient course. Rapid cycling is estimated to occur at some point in around 10% of patients with bipolar illness and is more common in women, those with early-onset illness and with comorbid substance misuse. A few people with rapid cycling alternate between periods of hypomania and major depressive disorder. However, it is far more common to have repeated and distinct episodes of depression dominate the picture such that persistent treatment-resistant depression is an important differential diagnosis. Antidepressant agents have poor efficacy in treating depression that occurs in rapid cycling illness and is thought to be a potential precipitant and/or maintaining factor. Therefore, many experts advise against the use of antidepressants in bipolar patients at risk of rapid cycling. Mood-stabilizing agents are the core of treatment for rapid cycling illness, often in combinations and sometimes with antipsychotic

agents. Adherence has been defined as 'the extent to which a person's behaviour, taking medication, following a diet, and/or executing lifestyle changes, corresponds with agreed recommendations from a health care provider'. It is also sometimes referred to as compliance or concordance. About half of the patients diagnosed with bipolar affective disorder become nonadherent during long-term treatment, a rate largely similar to other chronic illnesses. Nonadherence in bipolar affective disorder is a complex phenomenon determined by a multitude of factors. Four mutually interacting domains can be used to understand nonadherence: (i) patient (e.g. demographic characteristics such as younger age, comorbid substance use, lower socioeconomic group/social disadvantage and personal beliefs and attitudes around illness and treatment, which include insight levels); (ii) illness (e.g. greater severity of symptoms and/or frequency of episodes, earlier phase of illness); (iii) the effect of medications (e.g. side-effects); and (iv) characteristics of the clinicians (e.g. extent to which there is a truly collaborative relationship with patients).

Further reading **For a comprehensive review of the role of psychotherapy in bipolar affective disorder, see:** Lauder SD, Berk M, Castle DJ, et al. (2010) The role of psychotherapy in bipolar disorder. Medical Journal of Australia 193(S4):S31. doi:10.5694/j.1326-5377.2010.tb03895.x

Interventions that include psychoeducation, cognitive behavioural therapy, social rhythm therapy and family therapy have all been shown to impact positively upon adherence and relapse rates in bipolar illness. Interpersonal and social rhythm therapy is designed to help people with bipolar affective disorder improve their mood by understanding and stabilizing biological and social rhythms. It aims to create and sustain consistent daily routines (including habits and routines relative to medication), managing sleep/wake cycles and enhancing skills around managing, and where possible, avoiding socially based stressors. Storing up medication is a major concern, especially if it is deliberate. Lithium is one of the few psychotropic agents (along with clozapine) whereby receiving a prescription for it is associated with a reduced long-term risk of suicide. Beyond the stabilizing effect on illness course that many lithium users experience, the mechanism of action for this effect is not well understood. Lithium is a highly dangerous drug if taken in overdose, and it should be noted that 15% of patients with bipolar affective disorder die through suicide.

7. It emerges that Caroline had been reducing her lithium dose and missing doses because of an increasing preoccupation about her weight. This began after

her boyfriend suggested that she might consider starting a diet. She purchased some slimming pills but thought that she ought to check with her psychiatrist to clarify if they would be safe because a friend had told her that they could affect people with mental health problems.

- 16. How would you respond to these issues?
- 17. How are issues of weight control addressed in patients receiving psychotropic medications?

Weight gain is one of the main reasons that people diagnosed with depression and other mood disorders stop taking their medication. Many of the so-called slimming pills that are available have psychostimulant properties and, therefore, are best avoided in patients with bipolar affective disorder. These include products that contain diethylpropion, benzphetamine, methamphetamine, phentermine, phendimetrazine or topiramate. Moreover, there are more effective ways to achieve a sustained reduction in weight that involve careful consideration of prescribed medication. Often weight gain is dose-related or can be avoided by switching to agents within the same class. Overall, the largest body of research exists to support an association between weight gain and antipsychotic treatment (olanzapine and clozapine are especially implicated) and for antidepressants (e.g. mirtazapine). In addition, many services provide specific lifestyle programmes that focus upon helping patients to manage their diet better and engage with realistic exercise programmes that assist in weight management. Weight gain is greatest during acute treatment phases and in the first 3–6 months of treatment. The underlying mechanism behind weight gain in response to psychotropic treatment is unclear. For antipsychotics, an affinity for histamine H1 receptors, serotonin 5-HT2 and dopamine D2 receptor affinity have been identified. Weight gain with psychotropics is linked to a variety of factors: metabolic effects (e.g. hypertriglyceridemia, impaired glucose/insulin homeostasis, effects on leptin signalling), increased appetite and carbohydrate cravings and through decreased energy expenditure that can happen with reduced activity. Lithium may cause weight gain by an insulin-like effect on carbohydrate metabolism, altered fat cell metabolism and depressed thyroid function.

Further reading **For a comprehensive review of the epidemiology and management of metabolic issues in psychiatric patients, see:** Penninx BWJH, Lange SMM. (2018) Metabolic syndrome in psychiatric patients: overview, mechanisms, and implications. Dialogues in Clinical Neuroscience 20(1): 63–73.

Patients with mental illnesses such as schizophrenia and bipolar affective disorder have an increased prevalence of metabolic syndrome (approximately doubled) with a marked increase in the risk of cardiovascular disease and type 2 diabetes. This is an important factor in the marked gap in life expectancy of more than a decade between those with major functional psychiatric disorders, such as bipolar illness and schizophrenia, and the general population. The increased risk of metabolic issues is linked to a combination of lifestyle and medication effects. Moreover, regular monitoring of weight, abdominal girth and glucose and lipid parameters in collaboration with the patient's general practitioner are warranted

F4 Depressive disorders

1. Anna is a 22-year-old single mother of two children who presents to her general practitioner with abdominal discomfort. At consultation, the general practitioner notes that this is the third occasion that she has attended the surgery in as many weeks, having complained previously of back pain. Upon discussion, he notes that her complaints are quite vague and that she is ‘quiet’ throughout. When he asks how her mood has been, she begins to weep. She then explains that she has been upset since her recent split with her boyfriend.

- 1. What are your initial thoughts about this presentation?
- 2. What are the symptoms of ‘clinical depression’ and how is the severity of illness ascertained?

This presentation involves a combination of somatic symptoms and psychological distress. There are many possible interactions between physical and psychological complaints, and it is important to remain open-minded to the significance of either as a primary complaint. Pre-existing physical problems are often aggravated by psychological factors, while major psychological distress is often communicated through physical complaints (so-called ‘somatization’). This can lead to a delayed or misdiagnosis.

Further reading**For a key study that addresses the detection of depressive illness in primary care, see:** Arroll B, Khin N, Kerse N. (2003) Screening for depression in primary care with two verbally asked questions: cross sectional study. The British Medical Journal 327(7424):1144–1146. doi: 10.1136/bmj.327.7424.1144

Screening for possible depression is an important element of assessing patients with physical complaints, and this can be effectively managed by probing their recent mood and interest/enjoyment levels. These two symptoms (low mood

and anhedonia) are especially useful for identifying depressive illness in patients presenting to primary care. 'Clinical' depression is a term used to distinguish an abnormal state of sustained low mood as part of a wider syndrome of psychological and physiological disturbance that warrants specific therapeutic (or 'clinical') intervention rather than an expectation that time will allow for normal readjustment. In considering whether a patient has a clinical depressive illness, it is important to consider a range of symptom clusters that include: (1) low mood with loss of enjoyment and interest; (2) disturbed cognitive 'set' (negative self-regard, feelings of guilt or hopelessness); (3) somatic or biological features that reflect disturbance of biological rhythms (sleep/appetite/energy/libido); and (4) risk of self-harm. This constellation makes up the syndrome of clinical depression. The terminology used to describe depressive disorders in the International Classification of Diseases (ICD)-10 and Diagnostic and Statistical Manual of

Mental Disorders (DSM)-5 is somewhat different. ICD-10 categorizes depression as a depressive episode for single events and recurrent depressive disorder where two or more episodes occur. DSM-5 describes a spectrum of depressive disorders that includes major depressive disorder (including a major depressive episode), persistent depressive disorder (dysthymia), disruptive mood dysregulation disorder, premenstrual dysphoric disorder, substance/medication-induced depressive disorder, depressive disorder because of another medical condition, other specified depressive disorder, and unspecified depressive disorder. The common feature of all these disorders is the presence of a sad, empty, or irritable mood, accompanied by somatic and cognitive changes that significantly affect the individual's capacity to function. However, they differ in terms of duration, timing, or presumed cause.

ICD-10 includes three key symptoms and seven associated symptoms of depression. The key symptoms are: (1) persistent sadness or low mood; (2) loss of interest or pleasure; and (3) fatigue or low energy. The associated symptoms are disturbed sleep, poor concentration or indecisiveness, low self-confidence, poor or increased appetite, suicidal thoughts or acts, agitation or slowing of movements and guilt or self-blame. In ICD-10, the severity of depression is defined as not depressed (fewer than four symptoms), mild depression (four symptoms), moderate depression (five to six symptoms) and severe depression (seven or more symptoms, with or without psychotic symptoms) .

2. Anna reports that she has had a low mood for most of the day, every day of the previous month. She describes feeling guilty because she has been

struggling to care for her children and at times has been ‘snappy’ and irritable with them. She reports problems getting to sleep, poor appetite and concentration, loss of interest in her usual activities and that she has stopped going out except for essential trips (e.g. shopping for groceries). She denies any feelings of hopelessness or thoughts of self-harm. Her general practitioner suggests that she might benefit from antidepressant therapy, but she indicates that she would prefer to avoid ‘going down the medication route’. She agrees to contact the practice counsellor and return for another assessment in three weeks.

- 3. What are some suitable questions to explore for features of a major depressive illness?
- 4. What are the possible explanations for patients presenting with sadness, and how are they distinguished?
- 5. What is ‘counselling’, and what is the evidence to support its effectiveness in depressive illness?

Diagnosis of major depressive disorder:

1. Depressed mood and/or anhedonia (loss of interest or pleasure) that is present for most of the time and is pervasive in terms of personal, occupational and social functioning domains.

2. Associated symptoms that include:

• An altered sense of self with negative self-regard, feelings of worthlessness or guilt that can progress to include psychotic symptoms.

• Impaired thinking with reduced concentration and indecisiveness that can progress to the poverty of thought.

• Disturbed sleeping patterns (either insomnia or hypersomnia).

• Reduced energy with fatigue and/or reduced motivation.

• Reduced activity levels and/or agitation.

• Significant weight loss because of reduced interest in food or weight gain because of comfort eating.

A sense of pessimism and hopelessness that can progress to a passive death wish, thoughts of self-harm, suicidal ideation or intent.

3.That causes significant distress and/or impairment in functioning in social, interpersonal and occupational activities.

4.Symptoms are not better explained by substance use, medical illness or another functional psychiatric disorder (e.g. schizophrenia, schizoaffective disorder).

The severity of an episode is graded as mild, moderate and severe according to the number of the above features that are evident, with the presence of psychosis implying severe illness.

Suitable questions to explore for features of a major depressive illness include:

- How have you been feeling in your mood?
- Does your mood change over the day?
- Have you been able to enjoy things?
- How have you been feeling about yourself?
- How do you see the future?
- Describe your sleep pattern?
- What is your appetite like? Have you lost weight recently?
- How are your energy levels? Can you perform your usual activities?
- How has your concentration been? Can you follow a television programme or a newspaper article?
- Has there been any change in your libido?

It is a normal part of human experience to feel sadness in a variety of circumstances, but it is important to distinguish adjustment symptoms from more severe pathological states that warrant specific therapeutic interventions. While it is normal to experience sadness in response to adverse experiences and loss events, where such responses are more prolonged or symptomatically severe, this is likely to indicate psychological illness. A key consideration is to recognize that pathological states are usually precipitated by life events but also reflect a biological vulnerability towards illness. The 'understandability' of low mood needs to be carefully considered in the context of the possibility that such states may have progressed to become so severe as to now be beyond that which can be viewed as a normal reaction to adversity. In particular, the social divide between clinicians and patients from lower socioeconomic groups has been highlighted as a major obstacle to accurate detection of pathological states such as depression in such populations ('I would feel depressed if I had to deal with their day-to-day problems'). In the differential diagnosis, it is important to establish whether there are features of depressive illness, as this will take diagnostic precedence over adjustment reactions and requires therapeutic consideration. Depressive illness

commonly occurs in the context of physical illness (especially conditions that are chronic and/or impact upon neural function), and a comorbid physical cause is particularly important to consider where depressive illness first occurs in patients over 40 years of age.

Anxiety symptoms commonly complicate depressive illness and the appearance or a worsening of anxiety symptoms should always raise the possibility of an underlying depressive condition.

Bipolar depression is suggested by a personal history of elation (this should be carefully explored for in the previous history as undiagnosed milder episodes are not uncommon), a family history of bipolar illness, atypical clinical features (e.g. mixed mood states), severe illness and/or relative treatment resistance.

Dysthymia is a condition that presents with a persistent low mood of milder severity. Dysthymic individuals are often described by friends as 'grumpy', 'negative' or 'pessimistic'. 'Double-depression' relates to the occurrence of major depression in the context of long-standing dysthymia.

Further reading **For a review of the effectiveness of psychological interventions (including counselling) in depression, see:** Cape J, Whittington C, Buszewicz M, et al. (2010) Brief psychological therapies for anxiety and depression in primary care: meta-analysis and meta-regression. BMC Medicine 8:38. doi:10.1186/1741-7015-8-38

Counselling is the term used to describe talk therapy that can include a variety of elements (supportive, educational, coping skills enhancement) that assist and guide individuals in resolving personal, social, or psychological problems and difficulties. Therefore, counselling covers a wide range of possible supportive interventions, and the experience and training of the counsellor can vary widely. Evidence supports the effectiveness of counselling for mild and moderate depressive illness and subthreshold depression. Pharmacological interventions (often combined with psychological interventions) are recommended for more severe illness. The effectiveness of antidepressant agents in milder forms of depression is increasingly questioned as to whether they are superior to a placebo in clinical trials.

3. Anna attends the counsellor on a single occasion but fails to keep subsequent appointments. She returns for review three weeks later and describes some worsening of symptoms. At this point, she agrees to commence escitalopram 10 mg per day. Four weeks later, her condition has worsened, and she now confides that she has been feeling that she cannot shake the depression and having

intermittent thoughts of harming herself because she feels *'useless'* and *'a burden'* Upon questioning, she reassures the general practitioner that she could not harm herself because 'I love the children too much'. The general practitioner increases the dose of escitalopram to 15 mg per day, but after a further four weeks, she remains depressed and despondent about the future.

- 6. How does one select an appropriate antidepressant agent, and what is the recommended first-line pharmacological treatment for depressive illness?
- 7. What are the key messages to give to a patient commencing antidepressant therapy?
- 8. What are the indications for referral of depressed patients to specialist mental health services?

The choice of antidepressant agent is determined according to the severity of illness, previous history of antidepressant therapy and the potential for adverse effects and interactions with other medications. For the first episode of depression, a medication from the serotonin specific reuptake inhibitors (SSRI) family is generally considered appropriate because of their tolerability profile. If this strategy is not successful (with an adequate dosage for an adequate trial period), an agent from a different class, for example, a serotonin and noradrenaline reuptake inhibitor (SNRI), such as venlafaxine, should be considered.

Further reading **A good source of information for patients commencing antidepressant therapy can be accessed at:** http://www.rcpsych.ac.uk/mentalhealthinfoforall/problems/depression/antidepressants.aspx

Selecting antidepressants. Assess likely tolerability, including the following:

Anticipated adverse events, for example, side-effects and discontinuation symptoms. Potential interactions with concomitant medication. Comorbid physical illness.

The person's perception of the efficacy and tolerability of any antidepressants they have previously taken.

Usually choose a serotonin specific reuptake inhibitor in the first instance. **Take the following into account:**

Serotonin specific reuptake inhibitors are associated with an increased risk of bleeding. Consider prescribing a gastroprotective drug in older people who are taking nonsteroidal antiinflammatory drugs or aspirin.

For people who have a chronic physical health problem, consider using citalopram or sertraline as these have a lower propensity for drug interactions.

Paroxetine is associated with a higher incidence of discontinuation symptoms.

Consider toxicity in overdose for people at significant risk of suicide. Be aware that venlafaxine and especially tricyclic antidepressants are associated with a greater risk of death from overdose.

When prescribing drugs other than serotonin specific reuptake inhibitors, consider the following. The increased likelihood of the person stopping treatment because of side-effects, and the consequent need to increase the dosage gradually with venlafaxine, duloxetine and tricyclic antidepressants.

Specific warnings, contraindications and monitoring requirements for some drugs.

Some treatments should generally be prescribed by specialist mental health professionals:

Monoamine oxidase inhibitors (such as phenelzine).

Combination therapy with antidepressants.

Lithium augmentation of antidepressants.

When prescribing antidepressants for older adults. Adjust dosage, considering their physical health and concomitant medication. Monitor carefully for side-effects.

Nonadherence to antidepressant therapy is a common problem in everyday practice and is in part related to misinformation about the treatment process, including the timing of response and possible adverse effects. Patients commencing antidepressants should be encouraged to discuss their treatment expectations.

In particular, it is important to emphasize that antidepressants are not addictive, not known to have major long-term adverse effects, have a delayed onset of action of 10–14 days, should be continued for at least six months after symptom resolution (longer in patients with severe or recurring episodes) and should not be abruptly discontinued since they can have discontinuation effects. This latter problem is especially common with agents with short half-lives, such as paroxetine and venlafaxine. Although most patients with a depressive illness can be managed

in primary care, referral to specialist mental health services is appropriate for patients with a depressive illness where:

- there are urgent concerns regarding safety for the patient or others.
- the severity of illness is such that specialist opinion regarding management is required.
- the patient has a history of treatment resistance.
- there are diagnostic uncertainties or significant complicating factors, such as comorbidities or situational factors.

Further reading **For an overview of the management of depression, see:** Timonen M, Liukkonen T. (2008) Management of depression in adults. BMJ 336:435–439. doi: 10.1136/bmj.39478.609097.BE

4. Anna's general practitioner makes a referral to the local mental health services where she is assessed and noted to have moderate-to-severe depression because of the presence of marked lowering of mood and widespread disturbance of biological function. She agrees to try a different antidepressant treatment.

- 9. What is an adequate trial of antidepressant treatment?
- 10. What are the main classes of antidepressants, and how do they compare with regard to their mechanisms of action?

An adequate trial of antidepressant treatment involves administering a therapeutic dosage for six weeks as long as the patient remains fully compliant with the treatment. An advantage of the SSRI family of agents is that the starting dosages are typically at the lower end of the therapeutic dosage range. In contrast, the older tricyclic agents require a number of dose escalations to reach the therapeutic range and are often prescribed at subtherapeutic dosages. Venlafaxine shares this potential for failure of response because of the use of low/subtherapeutic doses, with 150 mg per day considered the lowest therapeutic dose in healthy adults.The main classes of antidepressant agents are shown in table 14.

SSRI, serotonin specific reuptake inhibitor; SNRI, serotonin noradrenaline reuptake; NaSSA, Noradrenergic and specific serotonergic antidepressants; NaRI, noradrenaline reuptake inhibitor; SARI, Serotonin antagonist and reuptake inhibitor; NDRI, Noradrenaline and dopamine reuptake inhibitor; MAO-I, Monoamine oxidase inhibitors; TCA, tricyclic antidepressants

The monoamine hypothesis of depression postulates that a deficiency or imbalance in monoamines is a primary factor in the pathophysiology of depressive illness. Antidepressant agents increase synaptic monoamine availability by three principal mechanisms: (1) blockade of reuptake molecules; (2) inhibition of

monoamine catabolism by monoamine oxidase; and (3) enhancement of monoamine release by reducing feedback inhibition to presynaptic auto-receptors.

Table 14. Antidepressant Medications and Mechanism of Action

Name	Mechanism of Action	Example
SSRI	Selective serotonin reuptake inhibitors	Fluoxetine, Paroxetine, Sertraline, Citalopram Escitalopram
SNRI	Serotonin and noradrenaline reuptake inhibitors	Venlafaxine, Duloxetine
NaSSA	Noradrenergic and specific serotonergic antidepressants	Mirtazapine
NaRI	Selective noradrenaline reuptake inhibitor	Reboxetine
SARI	Serotonin antagonist and reuptake inhibitor	Trazodone
Melatonergic agents	Enhances noradrenaline and dopamine release	Agomelatine
TCA	Serotonin and noradrenaline reuptake inhibitors	Clomipramine, Nortriptyline, Amitriptyline
NDRI	Noradrenaline and dopamine reuptake inhibitors	Bupropion
MAO-I	Monoamine oxidase inhibitors	Moclobemide, Phenelzine, Tranylcypromine

SSRIs inhibit 5HT reuptake and block 5HT-1a auto-receptors, and thus, increase serotonin availability and release. They have minimal effects upon H1, alpha-adrenergic and muscarinic receptors with negligible effects on sodium channels and are thus relatively safe in case of an overdose. The major side-effects of SSRIs are nausea and gastrointestinal upset, early agitation, sexual dysfunction and an increased propensity for bleeding.

SNRIs inhibit the reuptake of both serotonin and noradrenaline (and dopamine at higher doses). They have minimal effects on H1, alpha-adrenergic and muscarinic receptors.

Noradrenergic and specific serotonergic antidepressants block alpha-2 adrenergic receptors, and thus, increase the release of both noradrenaline and serotonin. They also block alpha-1 adrenergic receptors, leading to orthostatic hypotension, and H1 receptors, leading to sedation and weight gain.

Noradrenaline reuptake inhibitors specifically block noradrenaline reuptake.

Serotonin antagonist and reuptake inhibitors increase serotonin and are often used for their sedative properties.

Noradrenaline and dopamine reuptake inhibitors block noradrenaline and dopamine reuptake, e.g. bupropion, which is also used to reduce cravings in smoking cessation.

Agomelatine is an antidepressant agent that antagonizes 5HT-2 receptors (enhances the release of noradrenaline and dopamine) and is an agonist at melatonergic receptors (M1 and M2).

Tricyclic antidepressants act principally by blocking the reuptake of both noradrenaline and serotonin (and dopamine). The relative balance of noradrenaline versus serotonin effect varies (e.g. clomipramine is principally serotonergic while nortriptyline is mainly noradrenergic). They have many other neurochemical effects that cause unwanted effects, for example:

- Blockade of muscarinic cholinergic receptors potentially causing dry mouth, blurred vision, urinary retention, constipation and impaired attention.
- Alpha-1 adrenergic antagonism potentially causing orthostatic hypotension and dizziness.
- Histaminic-1 receptor blockade potentially causing sedation and weight gain.
- Sodium channel blockade potentially causing cardiac arrhythmia and seizures.

Currently, they are not commonly used because of their side-effect profile.

Monoamine oxidase inhibitors are irreversible blockers of MAO-A, and thus, can cause the accumulation of amines (e.g. tyramine) with hypertensive effects. This requires careful dietary management to avoid certain foodstuffs (so-called 'wine and cheese' interaction) and has implications for drug interactions. They are reserved for atypical depressive illness. Examples include phenelzine and tranylcypromine. Moclobemide is a reversible monoamine oxidase inhibitor carrying a reduced risk of major food and drug interactions. However, patients should still be advised to avoid large quantities of tyramine rich foods and sympathomimetic drugs.

Further reading **For a meta-analysis comparing antidepressant agents, see:** Cipriani A, Furukawa TA, Salanti G, et al. (2019) Comparative efficacy and acceptability of 21 antidepressant drugs for the acute treatment of adults with major depressive disorder: a systematic review and network meta-analysis. The Lancet 391(10128):1357–1366. doi:10.1016/S0140-6736(17)32802-7

The use of agents as first- or second-line treatments is generally dictated by the severity of illness and propensity for side-effects. Although in clinical practice it is noted that agents with dual monoamine action (e.g. SNRIs) are more effective

for more severe illness, the evidence from large studies (e.g. the STAR–D trial) and meta-analyses do not indicate major differences in their efficacy.

5. Anna commences venlafaxine 75 mg per day with a plan to escalate the dose over a week to 225 mg. After a month, she has improved somewhat, but still complains of low mood, anergia and low confidence. In particular, she continues to experience initial insomnia and believes that this is the cause of her low energy levels. She asks if she could be prescribed a 'sleeper' to overcome this problem.

- 11. What is the impact of increasing doses of venlafaxine?
- 12. How can depression-related insomnia be managed?

The dosage at which antidepressants have a therapeutic effect is a key consideration in treatment. The SSRIs can generally be commenced at dosages that have a therapeutic effect. However, for other agents, such as venlafaxine, duloxetine and the older antidepressants (e.g. tricyclic agents), there is a need to escalate dosages to minimize the propensity for adverse effects. Venlafaxine is an example where increasing effectiveness is linked to dose escalation. This has been explained in terms of neurochemical activity: at doses of 75 mg and 150 mg per day, the principal neurochemical effect is serotonergic, while at doses of 200 mg and over, the dual action is more evident with enhanced noradrenergic and serotonergic activity. With even higher doses, such as 300 mg and above, dopaminergic effects also occur. Insomnia is a frequent problem in patients with depression and may involve any of a number of patterns, most commonly initial insomnia and early morning wakening, but also middle insomnia and, in some cases, hypersomnia. It is important to note that both the amount and quality of sleep are affected. Sleep problems improve as depression resolves, but short-term symptomatic management of insomnia is frequently required. It is worth noting that depression has been described as a sleep disorder such that restoring a healthy sleep pattern can be a key step in resolving overall symptoms of depression. Careful attention to sleep hygiene, emphasizing daytime exercise and avoiding stimulants (e.g. caffeine) can be helpful. In addition, many antidepressants are inherently sedative (e.g. mirtazapine, TCAs, agomelatine). However, where these are not preferred (e.g. risk of overdose with TCAs), it may be prudent to use a short-term course of a hypnotic agent (preferably one with less propensity for dependency and/or a 'hangover' effect) or an antipsychotic sedative agent (e.g. low dose quetiapine) if there are concerns about dependency potential.

6. Anna's psychiatrist increases the dose of venlafaxine to 300 mg per day and prescribes a short (two week) course of a hypnotic (zolpidem). Over the following month, her depressive symptoms settle, and she discontinues the

hypnotic. At follow-up review, Anna is keen to discuss how long she will need to continue treatment, and whether she can decrease the dosage now that she is feeling better and how she can prevent a recurrence.

- 13. How would you address her questions regarding how long she should continue treatment, and at what dosage?
- 14. How does the risk of recurrence relate to the number of previous episodes?

Continuation pharmacotherapy for 6–12 months after the symptoms resolve is recommended for all patients with depression who respond to acute treatment with antidepressants. In addition, maintenance phase pharmacotherapy has demonstrated efficacy in preventing depressive recurrence for up to five years. The risk of further episodes with treatment discontinuation is predicted by the previous episode frequency with a relapse rate of 50% after one episode, 70% after two episodes, and 90% or more after three previous episodes. In general, studies suggest that maintenance treatment doses are similar to those that establish initial response ('the dose that gets you well keeps you well'). However, recurrent depressive disorder should be considered a dynamic state where the risk of further episodes is a function of the interaction of predisposing risk factors and exposure to precipitating environmental factors (e.g. major life events, loss experiences). Consequently, careful attention to baseline risk relating to lifestyle (exercise, diet, substance use), social and relationship issues and other ongoing stresses allows for a greater sense of empowerment and ownership of illness. Depression can thus be conceptualized as a vulnerability towards depressive symptoms when exposed to stressful precipitants.

7. Anna discontinues medications after six months but re-presents a year later with symptoms of a severe depressive illness associated with marked biological disturbance, but without thoughts of self-harm or psychosis. She is commenced on venlafaxine, and the dose is increased up to 300 mg over the following 4–6 weeks. Unfortunately, however, this has a minimal effect on her symptoms.

- 15. What are the treatment options at this point?
- 16. What is the implication of this episode for maintenance treatment in the future?

Treatment-resistant depressive illness is defined as the failure to respond to two adequate trials of antidepressant therapy (or one antidepressant trial and electroconvulsive therapy). In such cases, it is important to review the diagnosis carefully to establish if depression is the primary issue. It is important to review

the aetiological model for depression, focusing on possible perpetuating factors (e.g. substance use, physical illness, unresolved psychological or social factors). In addition, one should explore the patient's perspective of the treatment and likely adherence. Psychological interventions can be useful. If a treatment-resistant depressive illness is the preferred diagnosis, then a range of possible therapeutic options are available. The sequence by which these options are used is generally determined by patient factors and the preferences and previous experiences of the treating team. There is little robust scientific evidence to favour one intervention over another, and a process of trial and error often follows. Options include the following:

- 1. Increasing to high dosage therapy
- 2. Changing antidepressant agent/class
- 3. Augmentation with a mood stabilizer, such as lithium
- 4. Electroconvulsive therapy
- 5. Combination antidepressant therapy (e.g. venlafaxine–mirtazapine combination)
- 6. Augmentation with an antipsychotic, T3 or psychological therapies
- 7. Use of an MAOI (especially if atypical features, such as hypersomnia, hyperphagia or reversed diurnal mood variation, are present)
- 8. Light therapy (especially if the illness follows a seasonal pattern)

Further reading **For a systematic review of the impact of antidepressant maintenance therapy, see:** Machmutow K, Meister R, Jansen A, et al. (2019) Comparative effectiveness of continuation and maintenance treatments for persistent depressive disorder in adults. Cochrane Database of Systematic Reviews 5:CD012855. doi:10.1002/14651858.CD012855.pub2

This second episode, with severe illness and treatment resistance, emphasizes the need for sustained treatment when her symptoms ultimately resolve. It is estimated that continued antidepressant therapy reduces the odds of relapse by 70%, but the optimal duration of such treatment remains unclear.

F40 Anxiety disorders

1. Colin is a 33-year-old married man who works as a junior bank official and lives with his wife and two daughters. He was referred by his general practitioner after he presented seeking help to deal with 'stress and anxiety'. He is especially worried about an upcoming wedding in which he will be the best man for his brother and is afraid that he will not be able to deal with the responsibility of making a speech and meeting so many people.

- 1. What are your initial thoughts regarding this presentation?
- 2. What are the principal complaints that patients with anxiety disorders present with and how do these patterns assist the differential diagnosis?

It is not unusual for individuals with anxiety disorders to seek help many years after the onset of their problems and in the context of an acute stressor that has 'brought things to a head'. All but the most severe anxiety disorders can usually be managed through a range of adaptive responses, including many maladaptive behaviours. Speaking in public is a common fear, and it has been reported that more people fear this than death itself! This presentation only gives a vague clue as to the nature of Colin's problems. In general, anxiety problems are considered pathological, where they can be considered beyond the usual reactions to adverse life situations and have a discernible and significant impact upon socio-adaptive functioning. The principal patterns for anxiety symptoms include general symptoms of excessive and uncontrollable worrying about everyday life experiences and/or more specific fears relating to specific phenomena. Symptoms follow two main patterns:

1. Persistent mild-to-moderate severity in mental discomfort associated with physical symptoms of tension and 'generalized anxiety'.

2. Discrete episodes of more extreme fear associated with a sense of losing control ('panic').

The latter tends to be the more potent precipitants of help-seeking behaviour.

2. At the consultation, Colin describes a longstanding history of excessive worrying dating back to early adulthood. He describes problems with persistent tension, muscle aches and fatigue. He describes occasional episodes of losing control with fear–'like an explosion of anxiety'. This has occurred in stressful situations such as having to face scrutiny at work (e.g. presentations at management meetings). These episodes only occur in specific situations of perceived stress. He denies any avoidant behaviours and describes an active social life. He is worried that if things get worse, he could end up like his maternal aunt who became housebound because of 'a fear of open spaces'.

- 3. What are the likely diagnoses?
- 4. What investigations would you perform to identify/exclude any physical factors contributing to his symptoms?
- 5. What is a 'panic attack?'
- 6. What are the criteria for panic disorder and how does it compare with GAD?
- 7. What is agoraphobia and how does it relate to panic disorder?

The differential diagnosis for anxiety is broad and subject to a diagnostic hierarchy in which mood and other disorders take diagnostic precedence . A primary anxiety disorder is not the favoured diagnosis if symptoms occur principally in the context of a comorbid major mental illness, such as depression or a psychotic illness. Patients with longstanding anxiety problems often present when there has been an escalation of symptoms in the context of an emergent comorbid mood or other disorder. Comorbidities are very common among people with anxiety disorders, with 50% or more individuals typically reporting another disorder. Therefore, it is important to carefully assess the character of symptoms and their context. Patients with premorbid anxious personality profiles are more prone to syndromal or clinical anxiety disorders, and this pattern typically presents as an acute worsening of symptoms. Anxiety is a common feature of depressive disorders, and careful assessment for syndromal depressive illness is important. Anxiety can also be a feature of other states, such as distressing persecutory beliefs or experience of hallucinations in psychotic illness. A range of medical conditions and substance-related circumstances can also be relevant, and a detailed medical history, physical examination and documentation of medication exposure and substance use is fundamental for identifying the causes and/or precipitating factors for anxiety. Patients with primary anxiety disorders have a three-fold greater use of medical services (e.g. 25% of cardiovascular referrals and 50% of patients assessed for irritable bowel syndrome have panic disorder).

The physical differential is broad and includes:

- Endocrine disorders (e.g. hyperthyroidism, diabetes, hypoparathyroidism or hypoglycaemia)
- Anaemia
- Cardiovascular (e.g. arrhythmias, ischaemic, congestive cardiac failure, valvular disease including mitral valve prolapse)
- Seizure-related or central nervous system (CNS) pathological condition (e.g. TLE/vestibular nerve diseases)
- Respiratory disorders (e.g. asthma or chronic obstructive pulmonary disease)
- Gastrointestinal disorder (e.g. irritable bowel syndrome)
- Chronic pain
- Substance-related (e.g. exposure to stimulants, steroids, bronchodilators, dopaminergic agents, withdrawal from alcohol or sedative-hypnotics).
- Other conditions including porphyria, systemic lupus erythematosis (SLE), carcinoid syndrome and pheochromocytoma.

Further reading **For a review of anxiety disorders and their relationship to medical conditions, see:** Hoge EA, Ivkovic A, Fricchione GL. (2012) Generalized anxiety disorder: diagnosis and treatment. The British Medical Journal 345:e7500. doi:10.1136/bmj.e7500

The pattern of symptoms will direct appropriate investigations (which are often in themselves quite anxiogenic!). The investigations typically include the following: a full blood count, urea and electrolytes, thyroid function, liver function tests, an electrocardiogram, urinary drug screen and fasting blood glucose measurement. Further testing is guided by findings from the history and physical examination.

In addition, the family of anxiety disorders is broad and a clear diagnosis requires detailed consideration of the pattern of symptoms, focusing on precipitants and course. In generalized anxiety disorder (GAD), symptoms tend to be persistent and follow themes of excessive worrying about everyday circumstances, such as work, health, finances and domestic factors. In panic disorder, there is a history of panic episodes without a specific focus and associated anticipatory anxiety *(fear of the fear*) with avoidance behaviours. In agoraphobia, anxiety and panic occurs in response to circumstances that are perceived as being away from a place of safety (e.g. home) and often referred to as 'a fear of open spaces' or where ease of exit is uncertain (holidays, shopping, church, queues). In social phobia (or social anxiety disorder), anxiety relates to social situations where there is a fear of embarrassment, scrutiny or evaluation by others. Specific phobias relate to circumscribed irrational fears of animals, flying, blood and insects. In posttraumatic stress disorder, anxiety relates to triggers and re-experiencing phenomena. In obsessive–compulsive disorder, anxiety relates to obsessional thoughts and compulsive behaviours, which predominate. In other disorders, anxiety occurs in relation to fears about health and well-being (hypochondriasis) and abnormal beliefs about appearance or body image (anorexia nervosa and dysmorphophobia).

Further reading **For a review of social anxiety disorder, see:** Leichsenring F, Leweke F. (2017) Social anxiety disorder. New England Journal of Medicine 376(23):2255–2264. doi:10.1056/NEJMcp1614701

The character of anxiety symptoms can also provide some clues. Situational factors shape clinical features; for example, shortness of breath occurs primarily with agoraphobia, while blushing, sweating and trembling are more strongly associated with social anxiety disorder. Colin's symptoms point towards a

longstanding pattern of generalized anxiety punctuated by occasional panic episodes that seem to follow a pattern suggestive of social anxiety disorder.

The diagnosis of social anxiety disorder is based upon:

- 1. Persistent difficulties with fear and anxiety in social or other performance situations where the person is likely to come under scrutiny from others.
- 2. Anxiety may manifest as intense generalized anxiety and/or with panic episodes.
- 3. Anticipatory anxiety and avoidance occur when faced with the prospect of situations that are likely to provoke these responses.
- 4. The person has insight into the excessive or irrational nature of their symptoms.
- 5. These difficulties are associated with reduced functioning in social, personal or occupational activities.
- 6. The symptoms are not better explained by another mental disorder (e.g. paranoid illness), substance effects or physical illness.

A panic attack is a discrete period of marked fear or anxiety that is associated with a variety of cognitive and physical phenomena. Panic attacks are sometimes described as an 'explosion' of panic. Panic episodes can vary considerably in frequency and duration, but are usually preceded by a prodromal period of escalating fearfulness (10 minutes or so) before the actual full-blown attack, which is usually quite brief (minutes), but occasionally, will last longer. The symptoms of panic in the order of frequency are palpitations, pounding heart, tachycardia, sweating, trembling, shaking, dyspnoea, choking, chest pain and fear of passing out, collapsing, dying or going mad. Other features include chills or hot flushes, nausea, abdominal discomfort, dizziness or light-headedness. Experiencing a panic episode is often described as terrifying and is associated with subsequent anticipatory anxiety regarding a recurrence. This leads to a generalization of the issue as the person tries to make sense of it; for example, if the first attack occurs in a church, the person may experience anticipatory anxiety and avoid going back to the church. The core concern is usually one of being unable to escape to safety in, for example, queues, enclosed spaces, public transport, crowds or shopping. Essentially, it is 'fear of a fear'. Furthermore, 50% of individuals with panic attacks have associated agoraphobia. Nocturnal panic attacks are unusual and suggest a physical cause. However, if they do present, they usually occur during slow-wave sleep.

Further reading **For a review of panic disorder, see:** Katon W. (2006) Panic disorder. New England Journal of Medicine 354:2360–2367. doi:10.1056/NEJMcp052466

Criteria for a panic episode: The sudden occurrence of acute and severe anxiety that typically occurs over several minutes. The individual may experience a number of compelling physical and psychic symptoms because of psychological factors. Possible symptoms include the following: sweating, tremor, feeling hot or chills, dizziness or a sense of feeling faint or lightheaded, shortness of breath or a sense of smothering or choking, tachycardia, palpitations, chest tightness or pain, nausea, abdominal discomfort, paraesthesia (numbness or tingling sensations), derealization, depersonalization, fear of losing control, vomiting, being incontinent or going crazy and intense fear of something bad happening or dying. Typically, a panic episode will involve a combination of four or more of these symptoms.

Panic disorder is diagnosed when regular panic attacks cause distress and dysfunction. Previously, a minimum frequency was required, but it has been recognized that people with panic disorder can often avoid panic episodes through avoidance behaviours, and that adaptive impact is a better measure of severity than the actual frequency of episodes.

Agoraphobia is a variant of panic disorder where the focus of the fear is geographical and related to particular places or situations where ‘escape to safety’ is difficult, resulting in a fear of ‘being trapped’. Avoidant behaviour can result in a diminished social repertoire, and in more severe cases, patients can become restricted to their homes (described by Colin in his aunt’s condition as ‘housebound’). The distinction between panic disorder and agoraphobia remains contentious. Many scholars, in an attempt to understand and avoid further attacks, have conceptualized agoraphobia as the attribution of panic episodes to specific places or circumstances. In ‘pure’ panic disorder, the cause of the attacks is less readily attributable to specific situations, and they are often reported as spontaneous or paroxysmal.

In contrast, GAD refers to less acute but more persistent anxiety and includes general anxiety, excessive worrying and apprehension that are disproportionate to circumstances. Themes include everyday matters; for example, work, finances, relationships and health. A core element is that patients with GAD struggle to control worries (‘normal’ worrying can be rationalized and maintained within a manageable level).

Further reading **For a review of GAD, see:** Gale C, Davidson O. (2007) Generalised anxiety disorder. BMJ 334(7593):579–581. doi:10.1136/bmj.39133.559282.BE

In GAD, excessive worrying impacts the patient's quality of life and socio-adaptive functioning.

3. Further discussion reveals that Colin was 'always nervous as a child' and experienced an episode of depression in his early 20s during a period of unemployment, and later, had a recurrence in his late 20s during a dispute with a neighbour following an incident in which the neighbour's dog bit Colin's wife. His anxiety symptoms became much worse during these times, and he had stopped going out because of the fear of getting stressed. He reports that he has recently started to 'borrow' diazepam (Valium) tablets from his aunt when he experiences stressful situations at work but finds that these make him feel tired. He also reports having 'a few drinks' sometimes to steady himself before social occasions as he is very conscious of his tendency to blush, and that he has a noticeable tremor in his hands.

- What is the relevance of the use of diazepam (Valium) and alcohol in the manner described?
- 9.What do we know about the cause and pathophysiology of anxiety disorders?
- 10.What is their relationship to other mental health problems, such as mood disorders?

Diagnosis of GAD:

1. Excessive and persistent sense of worry and apprehension that is associated with psychic discomfort and physical symptoms that are of a generalized nature.

2. Typical symptoms include feeling on edge, restless, distracted, irritable, anxious or unable to relax, impaired concentration, fatigue, generalized muscle tension and disturbed sleeping patterns.

3. Symptoms that cause significant distress and/or impairment in the functioning of social, interpersonal and occupational activities.

4. Symptoms are not better explained by substance use, medical illness or another functional psychiatric disorder (e.g. another anxiety disorder, depressive illness, schizophrenia, schizoaffective disorder).

Substance misuse is common in patients with anxiety disorders and often reflects efforts to manage symptoms through self-medication. Both alcohol and benzodiazepines have rapid anxiolytic effects that make them attractive for the

acute management of anxiety but are associated with a variety of adverse effects (sedation, poor coordination, disinhibition and dependency potential) and also tend to result in worsening 'rebound' anxiety as their effects wear off. The use of these agents to deal with specific situations of social discomfort emphasizes the socio-phobic element of his difficulties. Given the prominent physical symptoms with a substantial situational context, it is hardly surprising that both genetic and environmental factors are implicated in the causation of anxiety disorders. The considerable comorbidity between different anxiety disorders is associated with many similarities in relation to perceived causation. The heritability of anxiety disorders has been estimated between 30% and 50%. Although twin studies and family clustering support some specificity for specific disorders, studies also indicate a more generalized vulnerability towards anxiety disorder with the specific pattern of symptoms shaped by environmental factors. Recent work has identified that a genomic duplication (DUP25) on chromosome 15 that occurs in 7% of the normal population is present in more than 90% of patients with panic disorder. From a psychological perspective, there are many similar themes about the genesis of anxiety disorders (e.g. they are more common in patients with 'anxious' personality profiles). They are thought to reflect adverse development experiences relating to abnormal attachment characterized by overprotective and/or emotionally cold parenting by anxiety-prone parents. They are also linked to early loss and traumatic experiences that impact a person's perception of the world as a predictably safe place. There are some differences in the dominant themes of each disorder. The theme of lack of control and a propensity to view ambiguous situations as threatening is particularly linked to GAD and is thought to underpin the excessive and generalized fearfulness of everyday experiences. For conditions that include panic attacks (panic disorder, agoraphobia and socio-phobia), a combination of biological vulnerability towards an extreme physiological anxiety response (panic) is coupled with situational factors through classical conditioning. Then, this relationship is maintained by operant conditioning through avoidance behaviours. There remains considerable debate about the relative importance of biological propensity versus environmental precipitants that underpin the primary approach to treatment (to pharmacologically reduce biological panic attack propensity versus addressing psychological aspects of the episodes). In reality, most patients have a longstanding illness at the time of presentation, and therefore, it is necessary to address the biology of anxiety and situational factors that serve to maintain illness. For specific phobias, there is much emphasis placed upon 'preparedness', while most foci for phobias have some potential danger and the

propensity to develop a fear may be based upon an evolutionarily imprinted survival instinct (e.g. spiders or wild animals).

Further reading **For a detailed review of neurobiological anxiety disorder studies, see:** Martin EI, Ressler KJ, Binder E, Nemeroff CB. 2009 The neurobiology of anxiety disorders: Brain imaging, genetics, and psychoneuroendocrinology. Psychiatric Clinics of North America 32(3):549–575. doi:10.1016/j.psc.2009.05.004

The neurobiology of anxiety disorders indicates much overlap. However, there are also specific findings in specific anxiety disorders. In general, studies have focused on exploring the autonomic nervous system reactivity and neuroendocrine stress response, serotonergic and other neurochemical systems, γ-aminobutyric acid (GABA)ergic mechanisms based on the impact of benzodiazepines, and disturbances of brain regions/circuitry that are linked to emotional processing and the fear response. Studies indicate disturbed functioning of autonomic reactivity (e.g. abnormal galvanic skin response) and the hypothalamic, pituitary, adrenal stress axis, but with increased reactivity (e.g. firing at locus coeruleus in response to anxiogenic agents such as yohimbine) in panic disorder, but normal baseline measures and diminished reactivity in GAD. Moreover, 30% of patients with GAD are nonsuppressors on the dexamethasone suppression test, which highlights its biological overlap with mood disorders. The effectiveness of serotonergic agents in anxiety disorders has encouraged studies on the serotonergic parameters. These have indicated diminished 5HT receptors and transporter binding on positron emission tomography in panic disorder and reduced serotonergic function (cerebrospinal fluid/platelet binding) in GAD. GABAergic function is suggested by the link to the mechanism of action of benzodiazepines, which have a specific binding site at GABA-A receptors and enhance GABAergic inhibition in the CNS. In addition, GABA antagonists are anxiogenic (e.g. flumazenil). Other studies have explored brain structures that are known to mediate emotional responses to stress and threats. These studies suggest overactivity of the so-called fear/anxiety circuit that includes the amygdala, hippocampus, periaqueductal grey, locus coeruleus, thalamus, cingulate and orbitofrontal areas. Neuroimaging studies have demonstrated increased right amygdala volume in GAD. In terms of epidemiology, the lifetime risk of panic disorder is 4%, having a panic attack is 8%, GAD is 3%–4%, specific phobias is 10% and social anxiety disorder is approximately 2%–13% (depending on the particular study and diagnostic criteria used). The epidemiology of anxiety disorders highlights their considerable overlap with other anxiety disorders, depressive illness and substance

abuse disorders. For example, comorbidity rates for panic disorder include two-thirds with depression, one-third with substance abuse disorder and half with social phobia.

4. Colin is keen to ‘ *get something to help with the wedding in 4 weeks’* . He also explains that he would like to engage with ‘any treatment that might help’ as he feels that these problems have been restricting his career progress. As an example, he explains that he constantly worries about small events at work (and at home) and tends to avoid situations that might involve being scrutinized by others. He has avoided taking on roles of responsibility even though he enjoys his work and would like to contribute more to the strategic side of the business.

- What treatment options are there for the short- and long-term management of his problems?
- What are the pros and cons of using benzodiazepines as a treatment?
- How can we decide upon the appropriateness of pharmacological and psychological treatments?

The management of anxiety disorders has two principal elements: (1) to reduce the propensity for ongoing anxiety/panic, and (2) to address and minimize any comorbid problems and maladaptive coping mechanisms, such as avoidance behaviours and substance misuse. This requires a detailed assessment of the scope and evolution of difficulties and often requires sustained therapeutic input to allow for combined pharmacological and psychological interventions. In the short term, it is important to explore and clarify the nature of any symptoms. An explanation of how physical symptoms related to stress can often prevent a spiral of increasing psychological distress and somatization in response to physical symptoms occurring in response to psychological stress. Many patients find simple interventions around anxiety management and relaxation training allow them to gain better control over their symptoms. Most pharmacological interventions have a delayed onset of action of between 2 and 4 weeks, and thus, the short-term use of benzodiazepines can allow symptom control in the early stages of treatment. Many patients report that having access to a remedy for anxiety (e.g. benzodiazepine) in itself reduces the fear of losing control and reduces the need to use such an option, although the use of benzodiazepines on an as-needed basis has been linked to a greater risk of subsequent dependency. Of note, benzodiazepines are only licensed for short-term use in anxiety disorders because of their adverse effects that include sedation, slurred speech, ataxia, cognitive dulling, potentiation and cross-tolerance with alcohol, dependence and recreational abuse potential. Use of benzodiazepines may also interfere with the benefits of psychological interventions.

Benzodiazepines should be generally avoided in patients with a history of dependence (e.g. alcohol) or those who have particular demands (e.g. working with heavy or complex machinery, driving) for optimal alertness, and those with a history of aggression or impulsivity. Long-term use in maintenance therapy should be reserved for more severe and intractable cases in which other pharmacological and psychological interventions have not been successful. In Colin's case, simple educational interventions and a short course of benzodiazepines can allow for symptom control/stabilization in the short-term, including in the lead up to the wedding that has been worrying him. For long-term management of anxiety disorders, a range of pharmacological and psychological approaches have demonstrated their efficacy, and in general, these have similar success rates with some evidence that combination therapy may be better than either alone. Most patients with moderate or severe symptoms receive both psychological and pharmacological inputs because anxiety disorders tend to run a chronic course, and achieving optimal symptom control often requires trialling a variety of interventions. The choice of treatment in individual patients is largely directed by their symptom pattern, treatment preferences, pattern of engagement with different interventions (e.g. attendance at psychological therapy sessions and medication compliance) and concerns regarding potential adverse effects with medications.

Cognitive behavioural approaches have demonstrated effectiveness for anxiety disorders. The content and focus of sessions differ according to the pattern of anxiety (generalized versus panic) and the actual focus of fears. In GAD, cognitive behavioural therapy (CBT) typically includes elements such as psychoeducation, symptom monitoring, relaxation training, symptom exposure and cognitive restructuring. A typical course spans 12–16 sessions. In panic disorder and agoraphobia, the principal psychological treatments include CBT (as above-mentioned, but also with habituation to fearful cues) and exposure (controlled *in vivo* exposure to panicogenic situations) or both. In cognitive restructuring, patients are assisted in identifying negative automatic thoughts and to challenge these misinterpretations and de-catastrophize by graded exposure. In socio-phobia, exposure is an important aspect of therapy, which involves graded exposure to anxiety-provoking situations until these are gradually mastered. Group approaches are favoured, along with social skills training. Confronting avoidances and cognitive restructuring to promote focusing externally rather than internally in social situations are also common elements. There is evidence to support the use of serotonin specific reuptake inhibitors (SSRIs), serotonin and noradrenaline reuptake inhibitors, monoamine oxidase inhibitors, azapirones, pregabalin and

older agents, such as imipramine and trazodone, in the treatment of anxiety disorders. The use of other agents, such as beta-adrenergic blockers, is less well-supported but preferred by some clinicians. These various approaches appear to have similar effectiveness (although well-designed comparison studies are lacking) and, hence, treatment choice is primarily determined by tolerability issues.

Further reading **Look up the National Institute for Health and Care Excellence guidelines for the management of anxiety disorders in adults** : NICE (National Institute for Health and Care Excellence). (2011) Generalised anxiety disorder and panic disorder in adults: management, CG113. Available at: http://guidance.nice.org.uk/CG113

Consequently, SSRIs are the preferred first-line treatment and have demonstrated efficacy across the anxiety disorder spectrum. The typical onset of action is 2–4 weeks. If using antidepressant agents, especially SSRIs, one needs to be aware of the potential for hyperstimulation in the early stages of treatment, which is linked to early treatment drop out. This can be minimized by gradual dose escalation.

The azapirones (e.g. buspirone) are indicated as second-line therapy and lack the sedative effects of benzodiazepines, have reduced dependency potential and do not potentiate the effects of alcohol. The onset of action is 2–4 weeks. Pregabalin is a GABA analogue that is classed as an antiepileptic agent. Long-term trials have shown continued effectiveness in anxiety disorders without the development of tolerance. Unlike benzodiazepines, it has a beneficial effect on sleep and sleep architecture, produces less severe cognitive and psychomotor impairment and has a low potential for abuse and dependence. Therefore, it may be preferred over benzodiazepine. It is increasingly considered as a first-line treatment option. As pharmacological and psychological interventions have similar effectiveness, the choice of treatment is guided by patient preference, adverse effects profile, previous response and adherence. Ultimately, the patient should dictate treatment because there is evidence that they are more likely to respond (possibly because of better adherence) to the treatment they most believe in.

5. Colin successfully manages the wedding without using benzodiazepines as after a discussion he recognizes the dangers of their sedative and potentially disinhibiting effects. He subsequently undergoes a trial of escitalopram and engages with a course of CBT. He also attends the local mindfulness group. Over the following six months, his symptoms settle, and he reports getting on much better in his work and personal life. He takes up squash to engage in regular exercise and minimizes his intake of alcohol without totally discontinuing it. He

contacts the service to request that his general practitioner manage his care. Two years later, he is re-referred for assessment with an acute exacerbation of symptoms.

- What are the principal diagnostic considerations at this point?

Several possible factors may be relevant to this recurrence of symptoms. Typically, symptoms will be related to a specific stressor or circumstance. However, it is important to consider the relationship between cause and effect (put another way, some events are independent of the illness process, whereas others are dependent upon it).

Colin's previous history of depression makes this an important differential, and careful assessment for depressive symptoms is required. Issues of ongoing treatment compliance and adherence to lifestyle practices (e.g. exercise and substance avoidance) need to be explored. It is important to consider the possibility of a physical illness underpinning his symptoms, even where such possibilities were previously ruled out.

6. It emerges that Colin had discontinued his medication 6 months ago and gradually stopped engaging in social situations. He had become more preoccupied with the hassles of life, leading up to a panic attack just before the re-referral. He agrees to recommence medication and attend 'top-up' sessions with a psychologist. Colin's condition again settles. He later attends with his wife wondering if he should again try to go for a period medication-free, as in retrospect he relates his relapse to some work stresses rather than discontinuing medications or other anxio-protective activities (e.g. regular exercise).

- What is the likely outcome of discontinuing medication?
- What is the prognosis for major anxiety disorders?

Once symptoms have stabilized the issue of optimal maintenance therapy often arises. The course of anxiety disorders is variable, but for many, the condition is persistent, and the focus of ongoing treatment is to achieve optimal symptom control and maximize socio-adaptive functioning. Patients in whom symptom control has been achieved with medication, symptom recurrence is very common on discontinuation. Evidence suggests that psychological interventions are associated with more enduring benefits, including reduced symptom propensity beyond the initial period following exposure (thus, contrasting with the chemical effect of pharmacological interventions). Therefore, treatment may be sequenced to use medications for stabilization, followed by psychological approaches for more enduring symptom control, and thus, enabling the reduction or discontinuation of the medications prescribed. Overall, the prognosis of anxiety disorders is quite variable. The majority of patients gain good symptom control and functional

recovery. However, 50% have persisting anxiety symptoms. A better outcome is associated with less severe symptoms, absence of comorbid disorders (personality, other anxiety disorders or substance abuse), 'good' or robust premorbid personality, strong social capital and active engagement with treatmen.

F1 ALCOHOLISM

Alcoholism is a progressive disease that develops in connection with prolonged abuse of alcohol with the formation of pathological attraction to alcohol, which is due to mental and then physical dependence on it. Change in alcohol tolerance is obliate symptom of alcoholism. The symptom of increasing tolerance is identified when the amount of alcohol initially consumed no longer causes the previous states of intoxication,so patient increase the dose by 2-3 times. In this case, protective emetic reflex vanishes, and intoxication of moderate or severe degree manifests. Alcohol abstinence syndrome (herenafter referred to as AAS, hangover) corresponds to alcohol deprivation syndrome. In this case, in the morning after drinking the alcohol the day before, the patient is in low spirit, as well as there are fixed ideas of elf-humiliation and self- accusation of their acts committed before; they feel physical ailment, weakness,palpitation, and heaviness in their head.

First stage manifests itself in pathological attraction to alcohol. Mental disorders manifest themselves in the form of neurasthenia-like symptoms: vegetovascular dystonia, disturbance in sleep and appetite are noted.

Second stage (addictive) is difficult for patient to concentrate; fatigue is present during intellectual work, as well as shortness of temper, anxiety, and various unpleasant somatic sensations. In the addictive stage, episodic psychotic disorders begin in form delirium, hallucinosis or paranoid.

Third stage (Encephalopathic) is accompanied by worsening of AAS. At this stage, various psychoses are more pronounced and epileptic seizures can be present. The tolerance to alcohol falls. Almost all patients have heavy drinking episodes or systematic drunkenness. Patients drink daily and cootinuously. All interests are reduced to drinking. The memory and intellect have degenerated very much; personality degradation is so severe that the patient loses interest in their occupation and work. At the final stage of the disesse many patients have apathy, inertia, ana inaction.

F6 Personality disorders (Psychopathies)

Personality disorders (Psychopathies) mean a stable pathology (deformation) of a person developing in childhood and been kept throughout their life. The pathology manifests itself in the disintegration of the personality, manifested at such an exent that it violates adaptation and complicates interpersonal relationships. Pathological reactions (decompensations) are a result of unpleasant life situations, stress, longtime overwork, and unimplemented expectations. The reactions themselves can be directed inwardly (which leads to internal conflict, neurosis) or outwardly (aggression, fixed ideas of persecution and querulous behavior).

The psychiatric history

Taking a good psychiatric history requires that the interviewer simultaneously attends to a variety of challenges, including facilitating the patient, observing patient behaviour while closely listening to what is said (and not said!) and how, and finding a balance between allowing the patient to tell their story while also interjecting to clarify particular points of note, as well as steering the conversation through the necessary components of a thorough history. It is important to plan such encounters and to make oneself aware of as much background information as possible as this can minimize any potential misunderstandings while also equipping the interviewer to demonstrate accurate empathy with the patient's perspective. It is important to remember that often patients have already had to explain their difficulties to other people before you engage with them, while some patients will have issues with paranoia and/or irritability. Sometimes, it may be necessary to have several interactions to obtain a full history.

A note on questioning style. Always begin with open questions. This facilitates the patient telling you their story in their own words and will yield more information than a litany of closed questions. Closed questions are appropriate to clarify or establish particular issues. An open question might be 'what are the main problems that you have been having?' or 'what has brought you to see me today?' Use closed questions to clarify specific points, for example, 'have you ever felt that life is not worth living?' or 'have you ever felt like harming yourself?' Leading questions, such as 'do you wake up earlier in the morning now?' should be avoided and a more, non-directive style should be employed, for example, 'can you describe your sleep?' This allows the patient to describe their experience more fully. It also avoids a situation where the patient is trying to give 'the right answer'

to please (or sometimes, mislead) the interviewer. The responses to leading questions about auditory hallucinations ('do the voices talk to each other about you?') or thought interferences ('do you have the experience of thoughts being placed into your head?') need to be interpreted carefully to avoid erroneously making a diagnosis of schizophreniform psychosis. Note that there is a marked difference between a patient responding with a simple 'yes' than 'yes, they make remarks about my behaviour'. It can be useful to consider questioning about risk, for example, as a series of ever-decreasing circles that start very open ('how have you been feeling about yourself?' and 'how do you see the future?') to becoming gradually more narrow in focus ('do you ever feel that life is not worth living or that you would not mind if you suddenly died?', to 'do you ever have thoughts of harming yourself in any way?'), to quite precise questions regarding thoughts of self-harm, self-harm behaviour and planning, and actual suicidal intent. Conducting an interview is like a dance–sometimes, it is a straightforward process wherein the patient is a willing and capable historian. At other times, it can be a more delicate process. It is important to try to avoid upsetting or annoying the patient, especially when patients are feeling irritable or paranoid. Some patients are frustrated that their beliefs are not being taken seriously enough or are doubted by others. In such cases, the experienced interviewer follows the general rule of patient interviewing 'neither collude nor collide'. This can be best achieved by empathizing with the patients' experience and emotional response rather than necessarily agreeing with delusional or other unusual ideas. Use of phrases, such as 'I'd like to try to understand that some more. Can you explain that in more detail?' or 'that sounds very difficult. How has that affected you?'

Setting the scene. It may sound obvious, but you should begin your interview by introducing yourself and any co-interviewers to the patient. In general, it is best to refer to the patient by title and surname in the first instance. Then, if the patient subsequently invites you to address them by their first name, you should do this. Ensure you know the names and relationships of anyone accompanying the patient and ask the patient if they would like them to remain in the room. Outline the purpose of the interview, explain confidentiality, and roughly how long the interview will take. As a general rule, it is useful to summarize the introductory discussion by saying that 'my task is to make it as easy as possible for you to tell your story and provide the information that can help us to establish how we can best help you'. Assure the patient that they can stop the interview at any time if they so wish, and that you are there to listen to their story and help them with their difficulties. Giving the patient a sense of control in this way helps to establish rapport. It is useful to establish who the primary help seeker is, for

example, a man with alcohol dependence may be presented as ‘my wife has threatened that she would leave if I didn’t do something about my drinking’ or a psychotic person may feel they were ‘forced’ to come by a parent or general practitioner (GP).

Introductions and demographics. This should include key sociodemographic details, such as name, address, date of birth, contact information, ethnic origin, GP details, next of kin and their contact information.

Presenting complaint. This should briefly encapsulate how the patient presented to you at this particular time, the source of referral and the patient’s description of their reason for seeking help and what they perceive as their main current difficulties. This is their subjective account of their ‘problem list’, and it should include quotes of the patient’s responses where possible. Typically, a principal problem list should contain no more than 3–4 ‘main problems’.

History of presenting complaint. This is a more detailed and specific analysis of the presenting problem and should include details on symptom duration, onset and progression and any identifiable triggers. The frequency of symptoms, and aggravating and alleviating factors, should be explored. One must establish the effect on functioning and the impact on the patient’s life. The interviewer should enquire if these symptoms were ever experienced in the past and, if so, what helped at that time. Use patient quotes liberally to represent the patient’s subjective account accurately. This can be useful to look back on at subsequent meetings to gauge progress. Moreover, it can be especially useful for other interviewers when assessing the patient subsequently. It is often useful to ask the patient ‘when were you last feeling well/your normal self?’ Longstanding difficulties raise the issue of temperament or personality as a factor. For example, a person with persistent low mood dating back to teenage years may have dysthymic disorder with or without a comorbid acute depressive exacerbation.

The importance of determining baseline functioning. Psychiatric interviewing is not straightforward and establishing what the patient is normally like allows you to determine how unwell they are or how far off baseline they have become. It is important not just to rely on a narrative account, such as ‘I was happier,’ but to ask the patient for examples of what they used to do that they are not doing now. Collateral history from someone who knows the patient well is also a good way to get a sense of a person’s baseline. Moreover, with acute presentations of major disorders, such as psychosis and mania, collateral history is sometimes the principal source of information. When information is gathered from

third parties, it should be documented in the psychiatric assessment together with details of the informant.

Past psychiatric history. Obtain a chronological list of previous psychiatric episodes/diagnoses with details of all inpatient, outpatient and GP care. Document whether inpatient care was voluntary or involuntary. Note specific treatments and the efficacy of these, for example, psychological, psychotropic medications and electroconvulsive therapy (ECT). Enquire about episodes of self-harm in the past and any treatment received. It is important here to document the patient's perspective on what they found helpful (or unhelpful) in the past.

Past medical and surgical history. Obtain a chronological list of diagnoses, treatments and consider possible relationships to psychiatric illness. Past medical and surgical history is important in terms of the cause of mental disorders (e.g. hypothyroidism and depressive illness, treatment with drugs, such as steroids and psychosis). It may also impact treatment choices because of cardiac status, pharmacokinetics and drug interactions .

Drug history. List all current medications using generic drug names together with the details on dose and frequency of administration. Note any previous psychotropic medications (and why these were discontinued) and any known drug sensitivities. Note that decisions around the choice of antidepressant and antipsychotic medications are strongly influenced by previous experiences of effectiveness and tolerability.

Family history. Include a family tree of the patient, siblings, parents and offspring documenting any psychiatric illnesses. For deceased relatives, document the age and cause of death. Enquire about a family history of suicide, alcohol and substance misuse. Relationships with family members should be explored and documented in this section. Moreover, it is increasingly recognized in pharmacogenetics that a family history of response to psychotropic medication can guide optimal choice for your patient.

Substance misuse. Ask the patient about their use of alcohol, street drugs, over the counter medications or drugs not prescribed for them. For each drug ask about the age of first use and longitudinal history, including quantity. It is important to try to clarify the recency of use. If appropriate, explore features of dependence.

Personal history

Early life and development. Document any known issues during pregnancy, delivery or in the postpartum period. Enquire about the attainment of developmental milestones, noting any delays (e.g. 'Did your mother/parents ever tell you that you had problems with walking or talking?'). Enquire about the family unit and the environment in the early years and any periods of separation or bereavement in childhood. As a general probe, it is useful to ask 'were you happy as a child?' and 'were you a good mixer? Did you make friends easily?'. It is useful to enquire about the style of parenting they received (e.g. strict, disciplinarian, loving) and any childhood adversity, such as significant losses, physical, emotional or sexual abuse and neglect. Note that there is a need to alert patients that you may be obligated to report disclosed historical child sexual abuse if the abuser is still alive or may pose a risk to others in any way.

Education. Document the patient's experience in primary and secondary school noting any bullying, conduct or other issues. Note academic performance and document the highest level of education reached. It is useful to explore the degree to which the patient engaged with extracurricular activities, such as sports, music, drama and other clubs, as this gives a sense of their character while growing up.

Occupational history. Give a chronological list of jobs the patient has held and reasons for leaving jobs and ask the patient to account for periods of unemployment.

Relationship history. Document current and major past relationships, durations of each and reasons for breaking up. If appropriate, enquire about sexual orientation. Ask about children, with whom they reside and the patient's relationship with them. In terms of current relationships, it is important to document the character of the relationship, especially in terms of whether it is close, supportive and confiding in nature as these are key aspects that are linked to vulnerability towards mental ill-health.

Social history. Ask about current accommodation and the patient's current financial situation. In particular, establish if there are any significant debts. Enquire about psychosocial stressors and social supports. Establish the daily activities of the patient and how this compares to previous baseline activities.

Forensic history. Obtain a chronological list of any interactions with law enforcement, any cautions, arrests, convictions and prison sentences. Furthermore, ask about any pending legal proceedings. Enquire about any violent offences or offences involving weapons.

Premorbid personality. Ask the patient what they are like when 'well', and to describe themself as a person–highlighting how others might describe them and enquiring about 'good' and 'bad' points. Specific questioning regarding introversion vs extroversion, obsessionality, perfectionism, moodiness and positivity in perspective, impulsivity (including incidences where this has been an issue) and spiritual/religious beliefs. It is important to realize that the patient's description may be unreliable as it tends to be coloured by their prevailing mental state. It may be more useful to ask how others would describe them or to rely on collateral sources of information.

Suggested probes to assess premorbid personality:

1. Are you outgoing or more of a home body?
2. Do you enjoy socializing, or do you generally prefer your own company?
3. How do you perform in groups – do you like to be at the centre of attention?
4. Do you have any perfectionistic traits?
5. How are you in terms of things like punctuality, order, cleanliness?
6. Do you sometimes spend too long on tasks when it is not necessary?
7. Are you normally a cautious person or do you like to jump straight in?
8. How long do you usually take when deciding about purchasing new items?
9. Have you ever got into trouble because of making rash decisions?
10. Are you generally positive or negative when thinking about everyday life?
11. Would you describe yourself as a glass half-full or half-empty person?
12. Do you suffer from mood swings or periods of persistent pessimism?

The Mental State Examination. The MSE is the process by which we document our observations of the patient's mental state at the time of the interview, including the presence and severity of mental symptoms, which are also known as psychopathological disturbances. It is cross-sectional and, in contrast to the psychiatric history, is objective rather than subjective. It is based upon all observations during the interview process. Much of the information documented under the MSE section is gathered or apparent during the general assessment

process; however, usually, these observations are supplemented by clarifying questions towards the end of the interview.

The Mental State Examination:

- Appearance and behaviour
- Speech
- Mood and affect (and risk assessment)
- Thinking (form and content)
- Perceptual disturbances
- Cognition
- Insight

The MSE is one of the key skills of psychiatry, and students must become familiar with the recognized scheme for describing the MSE. This is typically viewed as including seven separate sections (although there are subsections in each of these). It is important to follow the scheme in the correct order, and students may find the use of a mnemonic helpful to pin down the order (i.e. remember ASMTPCI). A widely suggested mnemonic is 'A Smart Medic Takes Particular Care Innately'. Some students find more quirky mnemonics connect better. A favourite in our programme was suggested by Dr Elizabeth Dunbar as 'A Saucy Maid Tickles People Coming In'. Just how and why they are tickled and where it is they are coming in to is uncertain but use whatever works best for you!

Appearance and behavior. Comment on the apparent age of the patient, physical appearance, demeanour, dress and level of self-care. These should be as objective as possible and neutral in tone (e.g. a person can be unusual in attire but should not be described as foolish or ridiculous–even if you perceive this to be the case!). Remember that it is important to be respectful of patients who present with unusual or odd behaviours, but that the clinician must navigate the territory between objective documentation while not trivializing or ignoring unusual behaviour. You should note the activity level of the patient during the interview, their spontaneity, level of eye contact, any agitation and general attitude to the interview. Comment on rapport–was the patient guarded or suspicious? Were they socially appropriate, cooperative, distractible, disinhibited or overfamiliar? Did the patient display any abnormal movements? Rapport is an important aspect of the assessment and should be considered as a two-way process. Sometimes students or training doctors may blame themselves for interviews that do not go well and in which they find it difficult to connect with the patient and form a productive rapport. It is important to note that one of the characteristics of psychosis is that it

includes experiences that are generally outside of normal experience and therefore frequently difficult for the assessor to fully empathize with. This is not the fault of the assessor however, merely an objective observation that it was difficult to establish good rapport during this interview and it also is an important factor in explaining circumstances where it is difficult to gather a full history as the patient is guarded or otherwise uncommunicative.

Speech. The patient's volume, tone and rate of speech should be noted. Ascertain whether the patient is a focused and fluent historian or if their speech is rambling, circumstantial or tangential. Take note of a reduced or increased amount of speech or any abnormal breaks in the conversation. Document any word-finding difficulties (such as nominal dysphasia) and document any abnormalities in the content of speech, such as personalized language (e.g. neologisms or metonyms: see section III, below). If you do not note any abnormalities, it is appropriate to comment on the relative negatives in your findings by stating 'speech was normal in flow, form and content'. Note that speech can be considered the audible expression of thinking, and it can be difficult at times to decide whether phenomena should be described as disturbances of thinking or speech. In general, disorders of speech content relate to the repetition of phrases or use of words in an unusual manner. Other disturbances of content (such as delusions or intrusive thoughts) are typically considered as disturbances to thought content. However, there is considerable flexibility in terms of in which cases these phenomena are reported–it is not unusual, for example, to comment at this point of the MSE that a patient with mania 'has evidence of pressurized speech with a flight of ideas and loosened associations' even though the latter two phenomena are more indicative of thought flow and form.

Mood, affect and risk assessment. It is important to document both the patient's subjective description of mood and your objective sense of their mood state. It is often useful to rate this in terms of score between 0 (unbearably low) to 10 (perfectly fine). At times there can be a disparity between the subjective and objective reporting of mood when a patient equates emotional discomfort (e.g. dysphoria) with depressed mood, which is typically a more pervasive and sustained phenomenon.

Questions to elicit low mood include the following:

- How have you been feeling in your mood?
- Does your mood change over the day?
- Have you been able to enjoy things?

- How have you been feeling about yourself?
- How do you see the future?

Questions to elicit elated mood include the following:

- How has your mood been recently?
- How good have you felt?
- Has your mood been changeable?
- How are your levels of confidence?
- Have you been feeling special, important or empowered?
- Does anything upset you?

Questions to elicit thoughts of self-harm include the following:

- How have you been feeling about the future?
- Have you ever felt that life is not worth living?
- Have you ever wished that you would not wake up?
- Have you ever thought that people would be better off without you?
- Have you ever thought about harming yourself or ending it all?
- Have you thought about how you might do it?
- Have you made any preparations?
- Have you tried to harm yourself?
- What would stop you doing it?
- Are you considering harming yourself at present?
- What methods have you considered?

Affect is the objective assessment of the patient's expression of their emotions. A description of the patient's affect in terms of range (e.g. flattening refers to the reduced range), appropriateness in expression (e.g. blunting refers to a lack of appropriateness to circumstances) and tone in terms of expression over time (e.g. labile if very changeable).

Thinking. During the MSE, we aim to get an appreciation of the patient's thinking in terms of: (1) stream (or flow); (2) form (or structure of thoughts, including their organization and how thoughts are connected); (3) content (the themes of thoughts, e.g. delusions, obsessions); and (4) possession of thought (whether the thoughts are 'interfered' with in any way, e.g. thought insertion, withdrawal, broadcasting). In terms of eliciting abnormal thought content and possession, it is often useful to begin with a question, such as ' *is there anything in particular on your mind at the moment* ?' or ' *has anything been bothering you lately?'* It can be useful to facilitate patients with the comment ' *Sometimes when people are unwell or stressed, they have unusual thoughts or experiences…* '

Questions that can used to explore for abnormalities of thought content and form:

• Are you ever worried that people are talking about you, following you or trying to harm you in any way? Who do you think is behind it (e.g. Mafia, MI5, ISIS, aliens)

Persecutory Delusion

• Have you ever felt you were under the control of some external force or power?

Delusion of Control / Passivity

• Has anything happened recently that has been very important for you? (e.g. the traffic light changed, and you realized you had been chosen to lead people) ***Delusional Perception***

• Did you experience a sense of perplexity where you had some sense of inexplicable change in your environment? You sensed 'Something is not quite right' ***Delusional Mood***

• Do you have a sense that people are paying attention to you? Do you ever receive messages from the television/radio/newspaper? ***Delusion of Reference***

• Do you feel you have committed a grave sin or crime? Do you deserve to be punished for that? ***Delusion of Guilt***

• Do you have any special gifts or power? Are you famous in any way? ***Delusion of Grandiosity***

• Do you ever feel you are 'made to' act or feel in a certain way? Do you ever feel that your thought or feelings are outside of your control? ***Passivity***

• Do you feel financially secure? Are others trying to take your wealth? ***Delusion of Poverty***

• Do you think something terrible has or will happen to you? Do you feel doomed? Do you ever feel part of your body is dead? ***Nihilistic Delusion***

• Are you able to think clearly now? Do you think your thoughts are being interfered with in any way?

1. For example, those thoughts are being put into your head… ***insertion***
2. or taken out… ***withdrawal***
3. or that others can hear your thoughts… ***broadcast***

• Do you ever draw a blank in your thoughts? Do your thoughts ever stop suddenly and unexpectedly when your thinking was fine moments before? ***Thought Block***

Perception. In this section of the MSE, we are interested in identifying abnormalities that the patient may be experiencing in any sensory modality. For both delusions and hallucinations, it is important to establish the degree of conviction. Useful questions include the following: Is it possible that you are mistaken? Do you think there could be another explanation? Could your mind be playing tricks on you?

Questions to elicit perceptual disturbances:

• Has it ever happened that you have heard a noise (***Elementary***) or a voice when there was nobody around to account for it?

• Just one voice or more? Male/female? Can you identify who they are?

• Do they talk to each other? … talk directly to you?

• Do they comment on what you are doing?

• Do you think they are coming from your own mind or can you locate where in the room they are coming from? Are you hearing them through you?

• Are they as clear as my voice?

• Can you stop them?

• When do they happen? (going to sleep / waking up)

• Do you feel they are real or could there be another explanation?

• Has it ever happened that you have **seen** something that others did not appear to see?

• Has it ever happened that you have felt something strange in your body, for example, someone touching you when no one was there? Electricity? Muscles being squeezed? Itching or a sense of there being insects under your skin?

• Has it ever happened that you have **smelled / tasted** something that others did not appear to smell / taste?

Cognition. The assessment of cognition begins as you first observe the patient and then progresses to include eliciting specific aspects of performance, usually with formal testing. Bedside testing of cognition can be supported by cognitive batteries, such as the mini-MSE or the Montreal cognitive assessment test, which have the added advantage of providing scoring systems that are linked to significant impairment. However, both tools are subject to restrictions in their use and assessment of cognition can be readily achieved through a systematic process of observing the patient and conducting some simple tests of each cognitive modality.

A scheme for bedside/office-based assessment of cognitive function.This includes commenting on their level of consciousness, orientation, attention, short and long-term memory, executive abilities and visuospatial functioning.

• How alert and aroused are they? What is their level of **awareness** of their environment and capacity to engage in a coherent conversation? (e.g. Can I ask you your name? Where are you from? Why are you in the hospital?)

• Assess **Orientation** to time, place and person (others and themselves). Typical questions include the following: What is your name? Where is this place? Why are you here? Can you tell me what day it is, and the date? What month (year) are we in? What do you think that I do for a living? Who is that person (key nurse) over there?

• Consider their **attention** levels–are they able to focus and sustain the conversation? Formally, test for attention using a simple test, such as the reciting the months of the year forwards (ability to focus attention) and backwards (ability to sustain attention). Generally, people under age 65 years should be able to recite the months backwards to January without error. For those over age 65 years, they should be able to recite the months of the year backwards to July with no more than one omission. Other tests of attention are less preferred as they involve aspects of cognition other than attention (e.g. serial sevens require mathematical ability; spelling 'world' backwards requires literacy) and are thus subject to bias. Counting back from 20 to 1 requires minimal mathematical ability and, is thus, impacted upon mostly by the ability to maintain attention to the task.

• **Short-term memory** can be assessed by asking the patient if they can recall your name (presuming that you have provided this at the beginning of the assessment!). More formally, you can document their ability to recall three words after a delay. This is done by asking them to acknowledge and recite three words (e.g. red, cat, ball), and then asking them to repeat this after five minutes has elapsed. It should be noted if the patient can recall the three words with or without specific cueing (e.g. 'can I give you a clue–it's a colour' or 'it's a type of animal'). Normal performance is to recall all three words. Short-term memory can also be assessed by a name and address (e.g. Mr John Green, 27 Main Street, Clonmel, Co. Tipperary).

• **Long-term or remote memory** can be assessed by asking about verifiable personal details (names of family members, operations they have undergone), which should be available in medical case notes and memory for well-known figures (e.g. who was the president before Michael D Higgins? Who was the Irish soccer manager at Italia 90? Who was the American president assassinated in 1963?).

• **Executive function** relates to abilities, such as organization and planning, concept formation and word/idea generation. This can be readily tested by asking the patient to generate as many words as they can beginning with a particular letter

in the alphabet (e.g. letter 'F') or animals that you might find in a zoo or types of motor car. It is usual to be able to reach ten words within a minute.

• **Visuospatial function** can be tested by asking the patient to identify the shape of objects in their environment, the relative distance between objects (e.g. which is closer, the television or the window?) and through formal tests, such as the ability to copy overlapping pentagons or insert a particular time into a circular clock. Note that these latter tests are impacted by motor skills.

When impaired performance is evident, it is usual to follow-up with a second test, and if they also perform poorly on this, formal and more detailed testing may be indicated. A patient with normal cognitive function can usually be described as follows: 'Ms Z readily engaged with the interview and was able to converse without any difficulties in terms of attention and concentration. Formal testing indicated that she was orientated to time, place and person, and she was able to recite the months of the year backwards without error. In terms of memory, she had a good short-term recall for three objects and also was able to recount her previous medical history accurately and name our most recent past president. Executive function appeared intact in terms of her ability to explain her story in a logical and sequenced manner and to list more than ten words beginning with 'F' within a minute. She completed the overlapping pentagons test indicating intact visuospatial abilities'. When there are impairments, the description can be amended accordingly.

Insight. There are several facets to 'complete insight', and it is better to avoid terms, such as 'insightless', as there are four principal elements (or levels) to insight that warrant clarification and few patients can be truly considered to be lacking insight. For the psychiatric assessment and future management, it is important to establish these four aspects of insight, namely:

1. Does the patient acknowledge that they have a problem?
2. Do they recognize that they are unwell?
3. Do they recognize their problems/experiences as symptoms, and are these symptoms attributed to psychological/psychiatric illness.
4. Does the patient believe they need help, and are they willing to accept treatment?

Note that insight is a key determinant of the need to consider involuntary treatment. Insight may be present for some symptoms and not for others, e.g. a patient may accept that they have schizophrenia but may not recognize a delusional idea as evidence of illness.

Formulation. A psychiatric formulation should attempt to explain why this patient is unwell, in this way, at this time.

Synopsis. It should begin with a synopsis of 2–3 sentences that include demographic details and salient features of the patient's history, MSE and physical examination.

Differential diagnoses. A discussion of differential diagnoses, with evidence for and against each differential, should be included. The provisional diagnosis should be identified.

Aetiological factors. A discussion of relevant aetiological factors utilizing a biological, psychological and social approach should be included. This should explore predisposing, precipitating and perpetuating factors. Of note, there may be substantial overlap in the content of the nine cells here, e.g. family history of mental illness may lead to biological, psychological and social predisposing, precipitating and perpetuating factors. Moreover, some cells may be empty. The purpose of the table is to help to pull together the key elements of the case in a logical way.

Management plan The proposed management plan should include any relevant investigations and discuss treatment in terms of immediate and longer-term treatments, again using a biological, psychological and social approach.

Prognosis. A patient-specific statement on short- and long-term prognosis should be included highlighting good and poor prognostic indicators and reflect the natural history of the diagnosed disorder, course of illness (acute versus insidious), initial and/or previous response to treatment, level of insight, compliance with treatment, family history of response to treatment, premorbid adjustment and relevant social supports or lack thereof.

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Glushchenko Vita Valentinovna**,**
Ilyashenko Natalya Nikolaevna

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