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8 Anxiety and stress-related disorders

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362 Chapter 8 Anxiety and stress-related disorders Introduction If schizophrenia is ‘the heartland of psychiatry’, then the neurotic dis orders surely make up much of the rest of the continent, in view of their prevalence in the general population (see Table 8.1) and the morbidity they cause. As unpopular as the term ‘neurosis’ has become (for a historical per spective, see E Historical perspective, p. 364), it is still retained in the ICD-10 in the rubric ‘neurotic, stress-related, and somatoform disorders’. DSM-5 has effectively carved up the neuroses into ‘anxiety disorders’, ‘obsessive–compulsive and related disorders’ (OCRD), ‘trauma- and stressor-related disorders’, ‘dissociative disorders’, and ‘somatic symptom and related disorders’. Here, we retain the use of ‘neuroses’ as shorthand for all these disorders but will use the subdivisions when talking about the particular disorders. We have all experienced anxiety symptoms, perhaps suffer from a par ticular ‘phobia’, or are a little bit obsessive about certain things, but to be clinically significant, these problems must be severe enough to cause marked distress and/or substantially interfere with our day-to-day lives. Because of the recognizable quality of some of the symptoms of neurotic disorders, it may be helpful to divide them into three categories. Table 8.1 Estimated 12-mth prevalence of psychiatric disorders in the general population of the European Union (2010)* Diagnosis (DSM-IV) Best estimate (%) Number of persons affected (in millions) Alcohol dependence 3.4 14.6 Psychotic disorders 1.2 5.0 Major depression 6.9 30.3 Bipolar disorder 0.9 3.0 Anxiety

disorders 14.0 61.5 Panic disorder 1.8 7.9 Agoraphobia 2.0 8.8 Social anxiety disorder 2.3 10.1 Specific phobias 6.4 22.7 Generalized anxiety disorder 2.6 8.9 Obsessive–compulsive disorder 0.7 2.9 Post-traumatic stress disorder 2.0 7.7

- Data derived from Eurostat Directorate General of European Commission (Eurostat 2010) re ported by Wittchen, HU, et al. (2011) The size and burden of mental disorders and other disorders of the brain in Europe 2010. Eur Neuropsychopharmacol. 21:655–679.

Introduction The common neuroses • Anxiety/phobic disorders: e.g. panic disorder, agoraphobia, GAD, specific (understandable) phobias (e.g. snakes, spiders), hypochondriasis, social phobia. • Stress-related disorders: e.g. acute stress reactions, adjustment disorder, PTSD. • OCD. The unusual neuroses (i.e. outwith 'normal' experience) • Anxiety/phobic disorders: e.g. 'non-understandable' phobias (e.g. dirt, feathers), dysmorphophobia. • 'Hysterical' conversion disorders. • Dissociative/depersonalization–derealization disorder. • Somatoform disorders. 'Culture-specific' disorders Seen only in certain populations: • Chronic fatigue syndrome (CFS)/eating disorders (E Anorexia nervosa 1: overview, p. 410). • Other 'culture-bound' disorders/cultural concepts of distress (CCDs). This chapter deals with anxiety, phobic, and stress-related disorders. Other disorders are covered in Chapter 18 (E pp. 864–875 conversion, somatiza tion, CFS, hypochondriasis, and dysmorphophobia), Chapter 9 (E pp. 410– 419: eating disorders), and Chapter 21 (E pp. 984-–991: CCDs). Points to note • Anxiety symptoms are common in the general population. • Comorbidity is frequent (other neuroses, depression, substance misuse, personality disorder). • Anxiety disorders may often present with physical symptoms. • Management will usually involve a combined approach (pharmacological and psychological).

364 Chapter 8 Anxiety and stress-related disorders Historical perspective The term 'neurosis' was coined by William Cullen in 1777, replacing 'illness of the nerves' (coined by Robert Whytt in 1764 to replace the old 'va pours') and meaning any disease of the nervous system without a known organic basis (which, at the time, also included epilepsy). Clinical descrip tions of neurotic symptoms can be found in the works of Hippocrates. However, the 'illness' later vanished under the cloak of both pagan and Christian beliefs, with typical symptoms attributed to the work of spirits, possession, or divine punishment. It did not resurface properly until the Renaissance (the 1500s) thanks (in part) to the witchcraft trials, when doc tors were called in to present diagnoses of known illnesses that could be mistaken for demonic possession (the first recorded 'medical defence'!). Although there was much debate, the brain became the final resting place as the organ most likely to be involved in the aetiology of the condition. The history of the neuroses is tightly bound to the (re)discovery of hypnosis (formerly the remit of faith healing). The work of Franz-Anton Mesmer (1734–1815)—mesmerism—and James Braid (1795–1860)— braidism—was brought to France by Azam in 1859, coming to the atten tion of Charcot, whose experiments with hysterics would have a profound influence on one particular assistant—Sigmund Freud. Freud's first paper, published in 1886, shortly after his return to Vienna, was of a case of 'trau matic hysteria' in a ♂ patient. It was his Studies on Hysteria, written with Josef Breuer and published in 1895, that provided the starting point of his subsequent major concepts of psychoanalytical theory—including repres sion, psychic reality, and the subconscious. The idea of repression of trauma (out of consciousness) and the ap pearance of 'defences' was highly influential, with the neuroses regarded as illnesses of the mind, needing psychotherapeutic treatment. Old arguments of emotional vs physical factors resurfaced in the aftermath of the World War I, as some authorities

found it difficult to attribute the illnesses seen in fit, healthy young men (who had indisputably experienced traumatic events) to conversion hysteria or phobic neurosis. The encephalitis lethargicans epi demic in 1919, and the presence of numerous ‘hysterical’ symptoms (e.g. convulsions, mutism, feelings of passion, obsessions/compulsions, spasms), argued in favour of at least some of the neuroses having an organic basis. In the 1920s, Walter Cannon proposed the concept of the ‘emergency reaction’, believing this ‘fight-or-flight’ response was mediated by the auto nomic nervous system. He also noted that the physiological responses were too slow to account for feelings and that some other ‘neural mechanism’ must be at work. The dominance of the behaviourists in psychology relegated emotion to just another ‘way of acting’ in a particular situation (albeit internally per ceived). Although an over-simplification, this led to the development of the ‘conditioning theory’ of anxiety. John Watson, the father of behav iourism, claimed to have produced an animal phobia in an 11-mth-old boy ‘little Albert’ by making a loud clanging noise whilst the boy was playing with a rat. Watson proposed that neuroses arose out of traumatic learning situations and then persist to influence behaviour throughout life. This was adapted by the 1930s to include the concept of ‘instrumental conditioning’

Historical perspective (association of an emotionally arousing stimulus and a neutral response), and, in the 1940s, Mowrer attempted to translate Freud’s theory of anxiety neurosis into the language of learning theory—responses that reduce anx iety are learnt—sometimes these reinforced behaviours may be aberrant, unhelpful, or simply bizarre and present as neuroses. ‘Avoidance’ was pos tulated as the behaviour that was reinforced due to successfully removing a ‘negative reinforcer’ (e.g. fear). These ideas led to the rational treatment of phobias with desensitization techniques. In the search for Cannon’s neural mechanism, neurophysiologists used lesioning experiments to identify the thalamus as a critical gateway for stimuli, and the hypothalamus as mediating the physiological response [via the hypothalamic–pituitary–adrenal (HPA) axis]—the Cannon–Bard theory. Other theories emerged over the years (e.g. the Papez Circuit, 1937), and understanding the emotional life of the brain remains at the forefront of research (see The Emotional Brain by Joseph LeDoux, 1998). Inviting as psychological explanations appeared, the late 1950s also her alded the arrival of the BDZs. ‘Tranquillizers’ (e.g. Miltown®, Librium®, Valium®) became the ‘housewives’ choice’, effectively treating a multitude of neurotic symptoms. Unfortunately, the indiscriminate use of these drugs led to them being demonized as causing dependence problems (despite evidence for their effectiveness when properly used). The advent of anti depressants artificially separated neurotic depression from the other neur oses, but nonetheless some utility was also seen in treating the anxiety disorders. A key study was the use of clomipramine in the treatment of OCD (see The Boy Who Couldn’t Stop Washing by Judith Rapoport, 1989). The fact that clomipramine was the most serotonergic of the TCAs paved the way for the second-generation antidepressants (the SSRIs) used in neur oses (previously thought only to be amenable to psychological approaches). Brain imaging demonstrated underlying functional changes in OCD pa tients [in the frontal cortex (left orbital gyrus) and bilateral caudate nuclei], which ‘normalized’ after successful treatment with medication (and inter estingly with CBT techniques, although this took longer). For many patients with panic attacks, structural and functional changes were found in the tem poral lobes. These findings resonated with the long-held observation that neurotic symptoms (e.g. anxiety, panic, somatic symptoms, depersonaliza tion/derealization) were often reported in other ‘organic’ conditions (e.g. temporal lobe epilepsy). Modern views are eclectic in their approach, e.g. the biopsychosocial model (E Figure 6.1, p. 256). For the neuroses, early environmental influ ences (including social factors like maternal

deprivation) can alter the sensi tivity of physiological stress responses in adulthood. Hence, the experience of stressors (psychological or physical) may lead (e.g. through the effects of stress hormones such as cortisol, and other neurophysiological mech anisms) to alterations in the structure and/or function of the brain, which, in turn, manifest as clinical symptoms (i.e. behavioural and/or emotional change).

366 Chapter 8 Anxiety and stress-related disorders Hyperventilation syndrome Essence Ventilation exceeds metabolic demands, leading to haemodynamic and chemical changes producing characteristic symptoms (dyspnoea, agita tion, dizziness, atypical chest pain, tachypnoea, hyperpnoea, paraesthe siae, and carpopedal spasm) usually in a young, otherwise healthy, patient.1 Hyperventilation syndrome (HVS), a relatively common presentation; may be mistaken for panic disorder. Considerable overlap, hence inclusion here: • 50–60% of patients with panic disorder or agoraphobia have symptoms of HVS. • 25–35% of HVS patients have symptoms of panic disorder. It may also be confused with other organic diseases, particularly of the car diorespiratory system, due to the physical symptoms manifest. Aetiology Unknown, but certain stressors provoke an exaggerated respiratory re sponse in some individuals [e.g. emotional distress, sodium lactate, caffeine, isoprenaline, cholecystokinin, and carbon dioxide (CO_2)]. HVS patients tend to use accessory muscles to breathe, rather than the diaphragm, resulting in hyperinflated lungs and perceived effort or dyspnoea when stressors induce the need to take a deep breath. This leads to anxiety and triggers further deep breathing, setting up a vicious cycle. Epidemiology ♂:♀ = 1:7, usually presents between 15 and 55yrs but can occur at any age (except infancy). Symptoms and signs • Cardiac: chest pain/angina [atypical of cardiac origin: may last hours, not minutes; often relieved by exercise; glyceryl trinitrate (GTN) ineffective], ECG changes (prolonged QT, ST depression or elevation, and T-wave inversion). • Respiratory: hyperpnoea, tachypnoea, dyspnoea, wheeze [bronchospasm secondary to low partial pressure of carbon dioxide in arterial blood ($PaCO_2$)]. Note: in chronic forms, hyperventilation may not be clinically apparent. • CNS [due to reduced cerebral blood flow (CBF) secondary to hypocapnia): dizziness, weakness, confusion, agitation, depersonalization, visual hallucinations, syncope or seizure (rare), paraesthesiae (usually upper limbs and bilateral), peri-oral numbness. • GI: bloating, belching, flatus, epigastric pressure (due to aerophagia), dry mouth (due to mouth breathing and anxiety). • Metabolic (due to electrolyte disturbance secondary to respiratory alkalosis): acute hypocalcaemia (signs: carpopedal spasm, muscle twitching, +ve Chvostek and Trousseau signs, and prolonged QT interval), hypokalaemia (with generalized weakness), acute hypophosphataemia (may contribute to paraesthesiae and generalized weakness). 1 Formerly known as Da Costa syndrome. Other archaic terms include: cardiac neurasthenia, cardiac neurosis, circulatory neurasthenia, disordered action of the heart (DAH), effort syn drome, hyperdynamic–adrenergic circulatory state, hyperkinetic heart syndrome, irritable heart, neurocirculatory asthenia, soldier’s heart, and vasoregulatory asthenia.

Hyperventilation syndrome Differential diagnosis Extensive. Diagnosis of exclusion—acute respiratory distress syndrome (ARDS), (venous) air embolism, asthma, atrial fibrillation (AF), atrial flutter, cardiomyopathy, chronic obstructive pulmonary disease (COPD), costochondritis, diabetic ketoacidosis (DKA), hyperthyroidism, meta bolic acidosis, methaemoglobinaemia, MI, nasopharyngeal stenosis, panic (and other anxiety) disorder, pleural effusion, pneumonia, pneumothorax, pulmonary embolism (PE), smoke inhalation, CO poisoning, withdrawal syndromes. Investigations • Unless there is a clear history of HVS, any first presentations of hyperventilation

should be referred for exclusion of serious underlying medical problems (E Differential diagnosis, see above). • These investigations may include full physical, FBC, U&Es, TFTs, glucose, Ca^{2+}, phosphate (PO_4), pulse oximetry, arterial blood gas (ABG) [in HVS: pH normal, $PaCO_2$ and bicarbonate (HCO_3) low], toxicology, ELISA, D-dimer (PE), ECG, CXR, and possibly ventilation/perfusion (V/Q) scan. • Repeating these investigations at later presentations should only be done if there are new clinical findings. Management Acute management If serious underlying pathology excluded, management includes: • Reassuring the patient. • Alleviating severe anxiety (e.g. use of BDZs). • Establishment of normal breathing pattern (instructing the patient to breathe more abdominally using the diaphragm; physically compressing the upper chest and instructing the patient to exhale maximally to reduce hyperinflation). 2 Note: use of rebreathing techniques (e.g. into a paper bag) is no longer recommended due to reports of significant hypoxia and death. This form of rebreathing may be unsuccessful anyway because very distressed patients have difficulty complying with the technique and because CO_2 itself may be a chemical trigger for anxiety. Further management • Education, e.g. hyperventilation, relaxation, and breathing techniques (‘provocation’ should only be performed in this setting). • Formal breathing retraining (usually provided by physiotherapists) is available in some centres. • β-blockers and BDZs may be of some use. Some success reported for use of antidepressants in preventing further episodes. • If there is clear psychiatric morbidity (e.g. anxiety or depression), this should also be specifically addressed.

368 Chapter 8 Anxiety and stress-related disorders Panic disorder 1: clinical features Essence • Panic attack: period of intense fear characterized by a constellation of symptoms (see Box 8.1) that develop rapidly, reach a peak intensity in about 10min, and generally do not last longer than 20–30min (rarely over 1hr). Attacks may be either spontaneous (‘out of the blue’) or situational (usually where attacks have occurred previously). Sometimes attacks may occur during sleep (nocturnal panic attacks; E Nocturnal panic attacks, p. 470), and rarely physiological symptoms of anxiety may occur without the psychological component (non-fearful panic attacks).2 • Panic disorder:3 recurrent panic attacks, which are not secondary to substance misuse, medical conditions, or another psychiatric disorder. Frequency of occurrence may vary from many attacks a day to only a few a year. Usually a persistent worry about having another attack or consequences of the attack (which may lead to phobic avoidance of places or situations; E Agoraphobia, p. 374) and significant behavioural changes related to the attack. Symptoms/signs (See Box 8.1.) • Physical symptoms/signs related to autonomic arousal (e.g. tremor, tachycardia, tachypnoea, hypertension, sweating, GI upset), often compounded by HVS (in 50–60% of cases; E Hyperventilation syndrome (HVS), p. 366). Box 8.1 Symptoms associated with panic attacks In order of frequency of occurrence: • Palpitations, pounding heart, or accelerated heart rate. • Sweating. • Trembling or shaking. • Sense of shortness of breath or smothering. • Feeling of choking or difficulties swallowing (globus hystericus). • Chest pain or discomfort. • Nausea or abdominal distress. • Feeling dizzy, unsteady, light-headed, or faint. • Derealization or depersonalization (feeling detached from oneself or one’s surroundings). • Fear of losing control or going crazy. • Fear of dying (angor animus). • Numbness or tingling sensations (paraesthesiae). • Chills or hot flashes. 2 ‘Panic’ derives from the Greek god Pan, who was in the habit of frightening humans and animals ‘out of the blue’. 3 ICD-10 and DSM-5 specify that panic attacks in panic disorder are unexpected, and not situational. DSM-5 now includes ‘Panic attack specifier’ for the presence of panic symptoms associated with any other mental disorder (not just the anxiety disorders).

Panic disorder 1: clinical features • Concerns of death from cardiac or respiratory problems may be a major focus, leading to patients presenting (often repeatedly) to emergency medical services. • Panic disorder may be undiagnosed in patients with ‘unexplained’ medical symptoms (chest pain, back pain, GI symptoms including IBS, fatigue, headache, dizziness, or multiple symptoms). • Thoughts of suicide (or homicide) should be elicited; acute anxiety (particularly when recurrent) can lead to impulsive acts (usually directed towards self). Note: risk of attempted suicide substantially raised where comorbid depression or alcohol or substance misuse. Epidemiology4 Lifetime prevalence [National Comorbidity Survey–Replication 2001–2002 (NCS-R)]: 1.5–3.7% for panic disorder, 7–9% for panic attacks. Rates much higher in medical clinic samples, e.g. dizziness clinics (15%), cardiac clinics (16–65%), HVS clinics (25–35%). Women are 2–3 times more likely to be affected than men. Age of onset has a bimodal distribution, with highest peak incidence at 15–24yrs and a second peak at 45–54yrs. Rare after age 65 (0.1%). Other risk factors include: being widowed, divorced, or separ ated; living in a city; limited education; early parental loss; and physical or sexual abuse. Comorbidity Agoraphobia (community surveys: 30–50%; psychiatric clinics: 75%), de pressive disorder (up to 68%), other anxiety and related disorders (up to 50%, e.g. social phobia, OCD), alcohol (up to 30%) and substance misuse, bipolar affective disorder (20%), medical conditions (e.g. mitral valve pro lapse, hypertension, cardiomyopathy, COPD, HVS, IBS, migraine). Differential diagnosis Other anxiety or related disorder (panic attacks may be part of the dis order), substance or alcohol misuse/withdrawal (e.g. amphetamines, caf feine, cannabis, cocaine, theophylline, sedative hypnotics, steroids), mood disorders, psychiatric disorders secondary to medical conditions, medical conditions presenting with similar symptoms (e.g. endocrine: carcinoid syn drome, Cushing’s disease/syndrome, hyperthyroidism, hypoglycaemia, hypoparathyroidism, phaeochromocytoma; haematological: anaemia; cardiac: arrhythmias (supraventricular), atypical chest pain, mitral valve prolapse, MI; respiratory: COPD, asthma, HVS; neurological: epilepsy— especially TLE, vestibular dysfunction). Investigations No specific tests for panic disorder; basic investigations should be per formed to exclude physical causes [e.g. FBC, U&Es, glucose, TFTs, ECG; if supported by history/physical examination: toxicology, Ca2+, urinary vanillyl mandelic acid (VMA)/plasma homovanillic acid (pHVA), echo, and EEG]. 4 Kessler RC, Chiu WT, Jim R, et al. (2006) The epidemiology of panic attacks, panic disorder, and agoraphobia in the national comorbidity survey replication. Arch Gen Psychiatry 63:415–24.

370 Chapter 8 Anxiety and stress-related disorders Panic disorder 2: aetiological models A number of theories, based primarily on successful pharmacological treat ment, explain the biological basis of panic disorder. • The serotonergic model: exaggerated post-synaptic receptor response to synaptic serotonin, possibly secondary to subsensitivity (reduced binding) at 5-HT1A receptors and 5-HT transporters, perhaps secondary to disturbances in serotonin transporter (5-HTTLPR) and promoter (SLC6A4) genes. • The noradrenergic model: i adrenergic activity, with hypersensitivity of presynaptic α2 receptors. (Locus caeruleus activity affects the HPA axis, and the firing rate is i in panic.) • The GABA model: d inhibitory receptor sensitivity (impaired GABA neuronal response to BDZs), with resultant excitatory effect. • The cholecystokinin–pentagastrin model: pentagastrin induces panic in a dose-dependent fashion in patients with panic disorder. Gene studies also implicate CCK gene polymorphisms in panic disorder (see Box 8.2). • The lactate model: postulated aberrant metabolic activity induced by lactate, from studies involving exercise-induced panic attacks (replicated by IV lactate infusion). • The false suffocation CO2 hypothesis: explains panic phenomena by hypersensitive brainstem receptors. Panic disorder occurs more frequently in

individuals with a raised pCO2, e.g. during sleep, during the premenstrual period, and due to respiratory disorders. • The cognitive theory postulates that panic disorder is due to a heightened sensitivity to internal autonomic cues such as tachycardia. • The neuroanatomical model: suggests that panic attacks are mediated by an overactive 'fear network' in the brain that involves the amygdala, hippocampus, periaqueductal grey, locus caeruleus, thalamus, cingulate, and orbitofrontal areas. 'Fear' is thought to occur through reciprocal activity that originates in the amygdala and is projected to the anterior cingulate cortex and/or orbitofrontal cortex. Other projections from the amygdala to the hypothalamus mediate endocrine responses.

Panic disorder 2: aetiological models Box 8.2 The genetic hypothesis Panic disorder has moderate heritability of around 25–50% (from family and twin studies). Most studies to date suggest that vulnerability is genetically determined and most likely multifactorial, but critical stressors are required to develop clinical symptoms (e.g. separation/ loss event, adjusting to a new role, relationship problems, physiological stress—childbirth, surgery, hyperthyroidism). Replicated linkages have been found with chromosomes 13q, 22q, 7p, and 9q31. Candidate genes include ADOR2A, 10832/T, CCK, and those coding for 5-HT1A, 5-HT2A, COMT, NPY1R, MAOA, HCRT (hypocretin), and linked to the CRH gene. Recent large GWAS have identified the neuropeptide S gene, the amiloride-sensitive cation channel gene, and the adenosine A(2A) genes as candidate genes, with 4q21 and 7p being considered the strongest candidate regions for panic- and fear-associated anxiety disorder loci.1 1 Logue MW, Bauver SR, Knowles JA, et al. (2012) Multivariate analysis of anxiety disorders yields further evidence of linkage to chromosomes 4q21 and 7p in panic disorder families. Am J Med Genet B Neuropsychiatr Genet 159B:274–80.

372 Chapter 8 Anxiety and stress-related disorders Panic disorder 3: management guidelines Combination of pharmacological and psychological treatments may be superior to single approach. Choice of initial approach will depend upon patient preference, past history of previous benefit, costs, availability, and local guidelines.5,6 For emergency treatment of a panic attack, see Box 8.3. Pharmacological Current evidence does not suggest any superior efficacy between SSRIs, SNRIs, BDZs, TCAs, and monoamine oxidase inhibitors (MAOIs). Other factors will determine the choice of medication (E Antidepressants, p. 276). • SSRIs: in the UK, citalopram (20–30mg), escitalopram (5–10mg), paroxetine (10–40mg), and sertraline (50–200mg) are all licensed for panic disorder (and recommended as first line by NICE). In view of possibly initially increasing panic symptoms, start with the lowest possible dose and gradually increase. Beneficial effect may take up to 12wks and require high doses. • Alternative antidepressants (unlicensed in the UK): SNRIs (e.g. venlafaxine), TCAs (e.g. imipramine, clomipramine), MAOIs (e.g. phenelzine)—thought by some clinicians to be superior to TCAs (for severe, chronic symptoms), RIMAs (e.g. moclobemide). • BDZs (e.g. alprazolam or clonazepam): not recommended by NICE. Should be used with caution (due to potential for abuse or dependence and cognitive impairment) but may be effective for severe, frequent, incapacitating symptoms. Use for 1–2wks in combination with an antidepressant may 'cover' symptomatic relief until the antidepressant becomes effective. Note: 'anti-panic' effects do not show tolerance, although sedative effects do. • Limited benefit: little evidence to support use of buspirone, bupropion, mirtazapine, inositol, reboxetine, antipsychotics, anticonvulsants, and, perhaps surprisingly, propranolol. • Second-line treatment: consider changing to a different class agent (i.e. TCA, SNRI, SSRI, MAOI), addition of BDZ (or a different BDZ), trial of bupropion, or for severe symptoms, an SGA (e.g. olanzapine). • If successful: continue treatment for 12–18mths before trial discontinuation (gradually tapering of dose over 2–4mths). Do not confuse 'withdrawal'

effects (10–20% of patients) with re-emergence of symptoms (50–70% of patients). If symptoms recur, continue for 71yr before considering second trial discontinuation. (Note: patient may wish to continue treatment, rather than risk return of symptoms.) 5 National Institute for Health and Care Excellence (2011) Generalized anxiety disorder and panic dis order in adults: management. NICE guidance [CG113]. M https://www.nice.org.uk/guidance/cg113 [accessed 20 June 2018]. 6 Baldwin DS, Anderson IM, Nutt DJ, et al. (2014) Evidence-based pharmacological treatment of anxiety disorders, post-traumatic stress disorder and obsessive-compulsive disorder: a revision of the 2005 guidelines from the British Association for Psychopharmacology. J Psychopharmacol 28:403–39.

Panic disorder 3: management guidelines Box 8.3 Emergency treatment of an acute panic attack • Maintain a reassuring and calm attitude (most panic attacks resolve spontaneously within 30min). • If symptoms are severe and distressing, consider prompt use of BDZs (immediate relief of anxiety may help reassure the patient, provide confidence that treatment is possible, and reduce subsequent ‘emergency’ presentations). • If first presentation, exclude medical causes (may require admission to hospital for specific tests). • If panic attacks are recurrent, consider differential diagnosis for panic disorder and address underlying disorder (may require psychiatric referral). Psychological • CBT—behavioural methods: to treat phobic avoidance by exposure, use of relaxation, and control of hyperventilation. Cognitive methods: teaching about bodily responses associated with anxiety/education about panic attacks, modification of thinking errors. • Psychodynamic psychotherapy: there is some evidence for brief dynamic psychotherapy, particularly ‘emotion-focused’ treatment (e.g. ‘panic- focused psychodynamic psychotherapy’) where typical fears of being abandoned or trapped are explored. Issues of comorbidity • In view of high levels of comorbidity, treatment of these conditions should not be neglected. • For the other anxiety disorders and depression, this issue is somewhat simplified by the fact that SSRIs and other antidepressants have been shown to be effective for these conditions too. However, behavioural interventions (e.g. for OCD, social phobia) should also be considered. • Alcohol/substance abuse may need to be addressed first, but specific treatment for persistent symptoms of panic ought not to be overlooked. Course • Most patients seeking treatment have already experienced chronic symptoms for 10–15yrs. • Untreated, the disorder runs a chronic course. • With treatment, functional recovery is seen in 25–75% after the first 1–2yrs, falling to 10–30% after 5yrs. Long-term, around 50% will experience only mild symptoms. • Poor responses associated with: very severe initial symptoms, marked agoraphobia, low socio-economic status, less education, long duration of untreated symptoms, restricted social networks (including loss of a parent, divorce, remaining unmarried), and presence of personality disorder.

374 Chapter 8 Anxiety and stress-related disorders Agoraphobia Essence Anxiety and panic symptoms associated with places or situations where es cape may be difficult or embarrassing (e.g. crowds, public places, travelling alone or away from home), leading to avoidance.7 • In DSM-5, agoraphobia is diagnosed irrespective of panic disorder. If both criteria are met, then both diagnoses should be applied. • In ICD-10, the presence or absence of panic disorder when in the agoraphobic situation may be specified, i.e. agoraphobia with(out) panic disorder. If panic disorder occurs in other situations, then both diagnoses should be applied. (Proposals for ICD-11 are similar.) Whether or not agoraphobia differs from panic disorder neurobiologically or simply represents a more severe form of panic disorder remains con troversial. The similarities of epidemiology, genetics, environmental pre cipitants, and effective treatments are hard to ignore.

NCS-R data (2006) suggest that pure agoraphobia does occur, but it is rarer than earlier epi demiological studies would suggest (e.g. the ECS), with a lifetime prevalence of 1.3% and ♂:♀ = 2:3. Epidemiology Prevalence (6mths) 2.8–5.8% (ECA); ♂:♀ =1:3; as for panic disorder, there is a bimodal distribution, with the first being somewhat broader (15–35yrs). In later life, agoraphobic symptoms may develop secondary to physical frailty, with an associated fear of exacerbating medical problems or having an accident. Aetiology • Genetic: both genetic and environmental factors appear to play a role. The predisposition towards overly interpreting situations as dangerous may be genetic, and some commentators suggest an ethological factor involving an evolutionarily determined vulnerability to an unfamiliar territory. First-degree relatives also have an i prevalence of other anxiety and related disorders (e.g. panic disorder, social phobia), alcohol misuse, and depressive disorders. • Psychoanalytical: unconscious conflicts are repressed and may be transformed by displacement into phobic symptoms. • Learning theory: conditioned fear responses lead to learned avoidance. Comorbidity Panic disorder, depressive disorder, other anxiety and related disorders (e.g. 55% also have social phobia), alcohol and substance misuse. Differential diagnosis Other anxiety and related disorders (especially GAD, social phobia, OCD), depressive disorders, secondary avoidance due to delusional ideas in psych otic disorders. 7 Literally ‘fear of the marketplace’ (Greek).

Agoraphobia Management • Pharmacological Antidepressants: as for panic disorder. In the UK, citalopram, escitalopram, and paroxetine are licensed for the symptoms of panic disorder, with or without agoraphobia. Unlicensed: some evidence for clomipramine (high dose). BDZs: Short-term use only (may reinforce avoidance)—most evidence for alprazolam/clonazepam/ diazepam. • Psychological Behavioural methods: exposure techniques (focused on particular situations or places), relaxation training, and anxiety management. Cognitive methods: teaching about bodily responses associated with anxiety/education about panic attacks, modification of thinking errors.

376 Chapter 8 Anxiety and stress-related disorders Simple or specific phobias Essence Recurring, excessive, and unreasonable psychological or autonomic symp toms of anxiety, in the (anticipated) presence of a specific feared object or situation (see Box 8.4 for glossary) leading, whenever possible, to avoid ance. DSM-5 distinguishes the subtypes: animals, natural environment, blood, injection, injury, situational, and ‘other’. Epidemiology Prevalence: (NCS-R) lifetime 12.5%, 12mths 8.7%, 6mths (ECA) 4.5–11.9%; ♂:♀ (all) = 1:3; animal/situational phobias may be more common in ♀; mean age of occurrence is 15yrs: onset for animal phobias 77yrs, blood/ injection/injury 78yrs, situational phobias 720yrs. Aetiology • Genetic: both genetic and environmental factors play a role. MZ:DZ = 25.9%:11.0%8 for animal phobia, situational phobia roughly equal suggesting a stronger role for the environment. • Psychoanalytical: manifest fear is the symbolic representation of an unconscious conflict, which has been repressed and displaced into phobic symptoms. Box 8.4 Specific phobias—the top 20

1. Arachnophobia—The fear of spiders
2. Ophidiophobia—The fear of snakes.
3. Acrophobia—The fear of heights.
4. Agoraphobia—The fear of open or crowded spaces.
5. Cynophobia—The fear of dogs.
6. Astraphobia—The fear of thunder/lightning
7. Claustrophobia—The fear of enclosed spaces.

8. Mysophobia—The fear of germs.
9. Aerophobia—The fear of flying.
10. Trypophobia—The fear of holes.
11. Carcinophobia—The fear of cancer.
12. Thanatophobia—The fear of death.
13. Glossophobia—The fear of public speaking.
14. Monophobia—The fear of being alone.
15. Atychiphobia—The fear of failure.
16. Ornithophobia—The fear of birds.
17. Alektorophobia—The fear of chickens.
18. Enochlophobia—The fear of crowds.
19. Aphenphosmphobia—The fear of intimacy.
20. Trypanophobia—The fear of needles. Source: data from M http://www.fearof.net [accessed: 20 June 2018]. 8 Kendler KS, Neale MC, Kessler RC, et al. (1992) The genetic epidemiology of phobias in women. The interrelationship of agoraphobia, social phobia, situational phobia, and simple phobia. Arch Gen Psychiatry 49:273–81.

Simple or specific phobias • Learning theory: conditioned fear response related to a traumatic situation, with learned avoidance (trigger to the conditioned response may be a reminder of the original situation). Observational and informational learning also appear to be important, and the 'preparedness' theory (Marks)9 suggests that fear of certain objects may be evolutionarily adaptive (related to survival of the individual or species), selectively acquired, and difficult to extinguish. Comorbidity The lifetime risk for patients with specific phobias experiencing at least one other lifetime psychiatric disorder is reportedly over 80% (NCS), particu larly other anxiety disorders (panic, social phobia) and mood disorders (mania, depression, dysthymia). However, rates of substance misuse are considerably less than in other anxiety disorders. Differential diagnosis Panic disorder (fear of having a further panic attack), agoraphobia, social phobia, hypochondriasis (fear of having a specific serious illness), OCD (avoidance/fear of an object or situation due to obsessional thoughts, ideas, or ruminations), psychosis (avoidance due to a delusional idea of threat—fears tend to be overly excessive). Management Psychological • Behavioural therapy: exposure is the treatment of choice—methods aim to reduce the fear response, e.g. Wolpe's systematic desensitization10 with relaxation and graded exposure (either imaginary or in vivo—best evidence for in vivo techniques). Recent studies have utilized virtual environments [virtual reality exposure (VRE)]. • Other techniques: reciprocal inhibition, flooding (not better than graded exposure), and modelling. • Cognitive methods: education/anxiety management, coping skills/ strategies, and cognitive restructuring—may enhance long-term outcomes. • Pharmacological: generally not used, except in severe cases to reduce fear/avoidance (with BDZs, e.g. diazepam) and allow the patient to engage in exposure. May reduce the efficacy of behaviour therapy by inhibiting anxiety during exposure. β-blockers may be helpful but reduce sympathetic arousal, not subjective fear. There is limited evidence for SSRIs (e.g. escitalopram, paroxetine), but clear secondary depression may require antidepressant treatment. Course Without treatment, tends to run a chronic, recurrent course. However, individuals may not present unless life changes force them to confront the feared object or situation. 9 Marks IM (1969) Fears and Phobias. New York, NY: Academic Press. 10 Wolpe J (1973) The Practice of Behaviour Therapy, 2nd edn. New York, NY: Pergamon.

 Social phobia (ICD-10)/social anxiety disorder (DSM-5) Essence Symptoms of incapacitating anxiety (psychological and/or autonomic), not secondary to delusional or obsessive thoughts and restricted to particular social situations, e.g. having a conversation, meeting strangers, eating or drinking in public, or public speaking, leading to a desire for escape or avoid ance (which may reinforce the strongly held belief of social inadequacy). Epidemiology Lifetime rates vary: 2.4% (ECA), 12.1% (NCS-R), 12-mth prevalence 6.8% (NCS-R); ♂:♀ for those seeking treatment (however, community surveys suggest ♂ > ♀); bimodal distribution with peaks at 5yrs and 11–15yrs (ECA)—often patients do not present until they are in their 30s. Aetiology Both genetic and environmental factors play a role. MZ:DZ = 24%:15%. The predisposition towards overly interpreting situations as dangerous may be genetic, whereas individual interpretations of social cues may be environmentally determined (i.e. the particular trigger for the conditioned fear response depends on the social situation in which the first episode of anxiety was experienced). Responses may be learnt from observing parents. Imaging studies show i activity in individuals with social anx iety in fear networks (prefrontal cortex, amygdala, hippocampus) during anxiety-provoking tasks. Response to antidepressants suggests there may be dysregulation of 5-HT, NA, or DA systems. Symptoms/signs Somatic symptoms include blushing, trembling, dry mouth, and perspiration when exposed to the feared situation, with excessive fear (which is recognized as such by the patient) of humiliation, embarrassment, or others noticing how anxious they are. Individuals are often characteristically self-critical and perfec tionistic. Avoidance of situations may lead to difficulty in maintaining social/sexual relationships, educational problems (difficulties in interactions with other students/oral presentations), or vocational problems (work in less demanding jobs, well below their abilities). Thoughts of suicide are relatively common. Comorbidity There is a high level of psychiatric comorbidity with the most common dis orders, including simple phobia, agoraphobia, panic disorder, GAD, PTSD, depression/dysthymia, and substance misuse. Differential diagnosis Other anxiety and related disorders (especially GAD, agoraphobia, OCD), poor social skills, anxious/avoidant personality traits, depressive disorders, secondary avoidance due to delusional ideas in psychotic disorders, and substance misuse. Management • Psychological: CBT, in either an individual or a group setting, should be considered as a first-line therapy (with SSRIs/MAOIs) and may be

Social phobia (ICD-10)/social anxiety disorder (DSM-5) better at preventing relapse. Components of this approach include relaxation training/anxiety management (for autonomic arousal), social skills training, integrated exposure methods (modelling and graded exposure), and cognitive restructuring. NICE guidelines recommend either the Clark and Wells model or the Heimberg model of individual CBT weekly over 4mths. Alternatively, supported use of a CBT-based self-help book either face-to-face or by telephone. • Pharmacological: β-blockers (e.g. atenolol) may reduce autonomic arousal, particularly for ‘specific social phobia’ (e.g. performance anxiety). For more generalized social anxiety, SSRIs [e.g. escitalopram (licensed: 10mg/day initially; range 5–20mg/day), fluoxetine (unlicensed), fluvoxamine (unlicensed), paroxetine (unlicensed), sertraline (licensed: 25mg/day, i to 50mg/day after 1wk; max 200mg/day)], SNRIs [e.g. venlafaxine (licensed: 75mg/day)], and MAOIs [e.g. phenelzine (unlicensed)] are significantly more effective. Other treatment possibilities include RIMAs [e.g. moclobemide (licensed: 300mg/day for 3 days, then 600mg/day in two divided doses)] or the addition of a BDZ (e.g. clonazepam, alprazolam) or olanzapine. There is limited evidence for anticonvulsants [e.g. gabapentin, pregabalin, levetiracetam, valproate (all unlicensed)], and buspirone appears clinically ineffective for

generalized social phobia. NICE recommends first line: trial of SSRI; second line: alternative SSRI or venlafaxine; third line: phenelzine or moclobemide.11,12 • Psychotherapy: if the patient declines CBT and pharmacological interventions or they have proved ineffectual, short-term psychodynamic psychotherapy may be offered over 6–8mths, with a focus on education, establishing a secure positive therapeutic alliance to modify insecure attachments, core conflictual relationships, shame, exposure to feared social situations outside therapy sessions, establishing a self-affirming inner dialogue, and improving social skills. Course • Without treatment, social phobia may be a chronic, lifelong condition. • Course does not appear to be related to gender, age of onset, duration of illness, level of premorbid functioning, lifetime history of anxiety, or depressive disorders. • Extreme childhood shyness and behavioural inhibition may be early manifestations of social phobia. • With treatment, response rates may be up to 90%, especially with combined approaches. • Medication best regarded as long-term, as relapse rates are high on discontinuation. 11 National Institute for Health and Care Excellence (2013) Social anxiety disorder: recognition, as sessment and treatment. Clinical guideline [CG159]. M https://www.nice.org.uk/guidance/cg159 [accessed 20 June 2018]. 12 British Association for Psychopharmacology Guidelines (2014) Evidence-based pharmacological treatment of anxiety disorders, post-traumatic stress disorder and obsessive-compulsive disorder: A revision of the 2005 guidelines from the British Association for Psychopharmacology. M https://www.bap.org. uk/pdfs/BAP_Guidelines-Anxiety.pdf [accessed 20 June 2018].

380 Chapter 8 Anxiety and stress-related disorders Generalized anxiety disorder 1—clinical features and aetiology Essence ‘Excessive worry’ (generalized, free-floating, persistent anxiety) and feel ings of apprehension about everyday events/problems, with symptoms of muscle and psychic tension, causing significant distress/functional impairment. Symptoms/signs (See Box 8.5.) Epidemiology Prevalence: 6mths (ECA) 2.5–6.4%, 12mths (NCS-R) 3.1%, lifetime (NCS- R) 5.7%; lowest in 18–29yrs (4.1%) and 60+ yrs (3.7%); highest 45–59yrs (7.7%); ♀ > ♂, especially early onset (associated with childhood fears and marital/sexual disturbance); later onset often after a stressful event; single (730% never marry); unemployed. Aetiology (triple vulnerability model)13 • Generalized biological vulnerability: • Genetic—modest role, shared heritability with depression. • Neurobiological—human studies limited. Animal work implicates the NA system: diminished autonomic nervous system responsiveness (? down-regulation of α2 receptors); HPA axis: loss of regulatory control of cortisol [71/3 of GAD patients show reduced cortisol suppression using the dexamethasone suppression test (DMST)]; amygdala and stria terminalis—possible sustained or repeated activation by corticotropin-releasing factor (CRF) due to stress; septohippocampal (‘behavioural inhibition’) system: sustained activation moderated by ascending 5-HT and NA systems; BDZ-GABA system: reduced expression of peripheral BDZ receptors due to high cortisol levels; other neurotransmitter systems: dysregulation of 5-HT systems, cholecystokinin (CCK-4 and CCK-8S). • Generalized psychological vulnerability: • Diminished sense of control—trauma or insecure attachment to primary caregivers, leading to intolerance of uncertainty. • Parenting—overprotective or lacking warmth, leading to low perceived control over events. • Specific psychological vulnerability: stressful life events—trauma (e.g. early parental death, rape, war) and dysfunctional marital/family relationships. Comorbidity Other anxiety disorders (simple phobias, social phobia, panic disorder), de pression/dysthymia, alcohol and drug problems, other ‘physical’ conditions (e.g. IBS, HVS, atypical chest pain). 13 Suarez L, Bennett SM, Goldstein CM, et al. (2008) Understanding anxiety disorders from a ‘triple vulnerability’ framework. In: Antony MM, Stein MB (eds). Handbook of Anxiety and Anxiety Disorders, pp. 153–72. New York, NY: Oxford

University Press.

381 GAD 1—CLINICAL FEATURES AND AETIOLOGY Box 8.5 Symptoms of GAD (present most days) • At least 6 months' history of excessive anxiety and worry, with marked tension and apprehension about everyday events and problems (e.g. work or school performance). • DSM-5: at least three (or one in children) out of: • Restlessness or feeling keyed up or on edge. • Easy fatiguability. • Concentration difficulties or 'mind going blank'. • Irritability. • Muscle tension. • Sleep disturbance. • ICD-10: at least four (with at least one from 'autonomic arousal') out of: • Symptoms of autonomic arousal—palpitations/tachycardia; sweating; trembling/shaking; dry mouth. • 'Physical' symptoms—breathing difficulties; choking sensation; chest pain/discomfort; nausea/abdominal distress. • Mental state symptoms—feeling dizzy, unsteady, faint or light-headed; derealization/depersonalization; fear of losing control, 'going crazy', passing out, dying. • General symptoms—hot flushes/cold chills; numbness or tingling. • Symptoms of tension—muscle tension/aches and pains; restlessness/inability to relax; feeling keyed up, on edge, or mentally tense; a sensation of a lump in the throat or difficulty swallowing. • Other—exaggerated responses to minor surprises/being startled. • Concentration difficulties/'mind going blank'—due to worry or anxiety; persistent irritability; difficulty getting to sleep due to worrying.

382 Chapter 8 Anxiety and stress-related disorders Generalized anxiety disorder 2—differential diagnosis and management Differential diagnosis 'Normal worries', depression, mixed anxiety/depression, other anxiety disorders (the anxiety is more focused), drug and alcohol problems, med ical conditions (see Box 8.6), side effects of prescribed medications (see Box 8.7). Management • Psychological: generally less effective than in the other anxiety disorders (lack of situational triggers); some evidence for CBT14 combining behavioural methods (treat avoidance by exposure, use of relaxation, and control of hyperventilation) and cognitive methods (teaching about bodily responses related to anxiety/education about panic attacks, modification of thinking errors). • Pharmacological: directed towards predominant anxiety symptoms: • Somatic symptoms—BDZs14 (e.g. lorazepam, diazepam, alprazolam). • Psychic symptoms—buspirone15 (beneficial effects may take 2–4wks). • Depressive symptoms— SSRIs14 (licensed—escitalopram 10–20mg/day, paroxetine 20–50mg/day), SNRIs (licensed—duloxetine 60–120mg/ day, venlafaxine 75–225mg/day), TCAs (unlicensed—imipramine, clomipramine), trazodone (licensed 75–300mg/day), mirtazapine (unlicensed—30mg/day). • Cardiovascular symptoms or autonomic symptoms—β-blockers (e.g. atenolol). • Other treatments—pregabalin (licensed—start 150mg/day; max 600mg/day; in divided doses—alone or as an adjunct to SSRI/SNRI), agomelatine (unlicensed—25–50mg/day), quetiapine16 (unlicensed— 150mg/day—alone or as an adjunct to SSRI/SNRI), trifluoperazine (unlicensed—2–6mg/day). • Physical: psychosurgery (very rare)—for severe/intractable anxiety. Course Chronic and disabling, prognosis generally poor, remission rates low (730% after 3yrs, with treatment); 6-yr outcome—68% mild residual symptoms, 9% severe persistent impairment. Often comorbidity becomes more signifi cant (esp. alcohol misuse), and this worsens the prognosis. 14 NICE recommends SSRIs as first-line treatment (+ CBT) and does not recommend BDZs for

> 2–4wks. See: National Institute for Health and Care Excellence (2011) Generalised anxiety disorder and panic disorder in adults: management. Clinical

guideline [CG113]. M https://www.nice.org.uk/ guidance/cg113 [accessed 20 June 2018]. 15 Buspirone should be considered as an alternative to BDZs when sedative effects are unwanted (e.g. drivers of vehicles, pilots, machine operators), in patients with a personal/family history of drug misuse, or for those already taking other CNS depressants. 16 National Institute for Health and Care Excellence (2013) Generalised anxiety disorder: quetiapine. Evidence summary [ESUOM12]. M https://www.nice.org.uk/advice/esuom12/chapter/Key- points-from-the-evidence [accessed 20 June 2018].

383 GAD 2—DIFFERENTIAL DIAGNOSIS AND MANAGEMENT Box 8.6 Medical conditions associated with anxiety-like symptoms • Cardiovascular system (CVS): arrhythmias, ischaemic heart disease (IHD), mitral valve disease, cardiac failure. • Respiratory: asthma, COPD, HVS, PE, hypoxia. • Neurological: TLE, vestibular nerve disease. • Endocrine: hyperthyroidism, hypoparathyroidism, hypoglycaemia, phaeochromocytoma. • Miscellaneous: anaemia, porphyria, SLE, carcinoid tumour, pellagra. Box 8.7 Prescribed medications causing anxiety-like symptoms • CVS: antihypertensives, anti-arrhythmics. • Respiratory: bronchodilators, α1/β-adrenergic agonists. • CNS: anaesthetics (pre-med and post-general anaesthetic syndrome), anticholinergics, anticonvulsants, anti-Parkinsonian agents, antidepressants, antipsychotics (akathisia), disulfiram reactions, withdrawal from BDZs and other sedatives and hypnotics. • Miscellaneous: levothyroxine, NSAIDs, antibiotics, chemotherapy.

384 Chapter 8 Anxiety and stress-related disorders Obsessive–compulsive disorder 1—clinical features Essence A common, chronic condition, often associated with marked anxiety and depression, characterized by ‘obsessions’ (E Dictionary of psychiatric symptoms, p. 115) and ‘compulsions’ (E Dictionary of psychiatric symp toms, p. 104). Obsessions/compulsions (see Box 8.8) must cause distress or interfere with the person’s social or individual functioning (usually by wasting time) and should not be the result of another psychiatric disorder. At some point in the disorder, the person recognizes the symptoms to be excessive or unreasonable. In DSM-5, OCD is now within a separate category ‘Obsessive– compulsive and related disorders’, which includes body dysmorphic disorder (E Body dysmorphic disorder, p. 872), hoarding disorder (E Hoarding disorder (DSM-5), p. 389), trichotillomania (hair-pulling disorder) (E Trichotillomania (ICD-10/11; DSM-5), p. 425), excoriation (skin-picking) disorder (E Excoriation (skin-picking) disorder (DSM-5; ICD-11), p. 425), substance/medication-induced obsessive–compulsive and related disorder, and obsessive–compulsive and related disorder due to another medical condition. ICD-11 is likely to take a similar view with the proposed ‘Obsessive– compulsive and related disorders’, including OCD, body dysmorphic dis order, olfactory reference disorder (E Olfactory reference disorder (ORD), p. 388), hypochondriasis, hoarding disorder, body-focused repeti tive behaviour disorders (trichotillomania, excoriation disorder), and other specified obsessive–compulsive and related disorder. Box 8.8 Common obsessions and compulsions Obsessions • Contamination. • Order or symmetry. • Safety. • Doubt (of memory for events or perceptions). • Unwanted, intrusive sexual or aggressive thoughts. • Scrupulosity (the need to do the right thing or fear of committing an error, breaking the law, or religious transgression). Compulsions • Checking (e.g. doors, windows, electric sockets, appliances, safety of children). • Cleaning or washing excessively. • Counting or repeating actions a specific number of times. • Arranging objects in a specific way. • Touching or

tapping objects. • Hoarding (E Hoarding disorder (DSM-5), p. 389). • Confessing or constantly seeking reassurance. • Continual list-making.

Obsessive–compulsive disorder 1—clinical features Epidemiology Mean age: 20yrs, 70% onset before age 25yrs, 15% after age 35yrs, ♂ = ♀, prevalence: 0.5–3% of general population. Aetiology • Neurochemical: dysregulation of the 5-HT system (possibly involving 5- HT1B or 5-HT/DA interaction). • Immunological: cell-mediated autoimmune factors may be associated, e.g. against basal ganglia peptides—as in Sydenham's chorea. • Imaging: CT and MRI: bilateral reduction in caudate size. PET/SPECT: hypermetabolism in orbitofrontal gyrus, basal ganglia (caudate nuclei), and cingulum that 'normalizes', following successful treatment (either pharmacological or psychological). • Genetic: suggested by family and twin studies (3–7% of first-degree relatives affected; MZ: 50–80%, DZ: 25%), no candidate genes as yet identified, but polymorphisms of 5-HT1B have been replicated. • Psychological: defective arousal system and/or inability to control unpleasant internal states. Obsessions are conditioned (neutral) stimuli, associated with an anxiety-provoking event. Compulsions are learnt (and reinforced), as they are a form of anxiety-reducing avoidance. • Psychoanalytical: Freud coined the term 'obsessional neurosis', thought to be the result of regression from oedipal stage to pre-genital anal– erotic stage of development as a defence against aggressive or sexual (unconscious) impulses. Associated defences: isolation, undoing, and reaction formation. Symptoms occur when these defences fail to contain the anxiety. Associations Avoidant, dependent, histrionic traits (740% of cases), anankastic/ obsessive–compulsive traits (5–15%) prior to disorder. In schizophrenia, 5– 45% of patients may present with symptoms of OCD (schizo-obsessives— poorer prognosis). Sydenham's chorea (up to 70% of cases) and other basal ganglia disorders (e.g. Tourette's syndrome, post-encephalitic Parkinsonism). Comorbidity Depressive disorder (50–70%), alcohol- and drug-related disorders, social phobia, specific phobia, panic disorder, somatoform disorders, eating dis orders, impulse-control disorders (trichotillomania, kleptomania), PTSD, tic disorder (740% in juvenile OCD), Tourette's syndrome, suicidal thoughts or behaviours. Differential diagnosis 'Normal' (but recurrent) thoughts, worries, or habits (do not cause distress or functional impairment); anankastic personality disorder/OCD; schizo phrenia; phobias; depressive disorder; hypochondriasis; body dysmorphic disorder; trichotillomania.

386 Chapter 8 Anxiety and stress-related disorders Obsessive–compulsive disorder 2—management Management • Psychological: • CBT—recommended by NICE,17,18 but essentially takes a behavioural approach, including exposure and response prevention (ERP). • Behavioural therapy—response prevention useful in ritualistic behaviour; thought stopping may help in ruminations; exposure techniques for obsessions. • Cognitive therapy—so far not proven effective. • Psychotherapy—supportive: valuable (including family members, use of groups); psychoanalytical: no unequivocal evidence of effectiveness (insight-orientated psychotherapy may be useful in some patients). • Pharmacological: • Antidepressants SSRIs (licensed): escitalopram (10–20mg/day), fluoxetine (20–60mg/day), fluvoxamine (100–300mg/day), sertraline (150mg/day), or paroxetine (40–60mg/day) should be considered first line (no clear superiority of any one agent, high doses usually needed, at least 12wks for treatment response, long-term therapy). Clomipramine (e.g. 250–300mg) has specific anti-obsessional action (NICE second-line choice). Other (unlicensed) agents include citalopram (20–60mg/day; NICE recommended alone or in combination with clomipramine), venlafaxine (225–300mg). • Augmentative strategies: antipsychotic (risperidone, haloperidol, pimozide)—esp. if psychotic features, tics, or schizotypal

traits (less evidence for olanzapine, quetiapine, aripiprazole, paliperidone); buspirone/short-term clonazepam (not NICE recommended)—if marked anxiety; other possible adjunctive agents include mirtazapine (15–30mg), lamotrigine (100mg/day), topiramate (100–200mg/day), memantine (20mg/day), celecoxib (400mg/day), and dexamfetamine (30mg/day) or caffeine (300mg/day).19 • Physical: • ECT—consider if patient suicidal or severely incapacitated. • Psychosurgery—may be considered for severe, incapacitating, intractable cases (i.e. treatment-resistant: two antidepressants, three combination treatments, ECT, and behavioural therapy) where the patient can give informed consent, e.g. stereotactic cingulotomy (reported up to 65% success). In theory, disrupts the neuronal loop between the orbitofrontal cortex and basal ganglia. • DBS—efficacy remains to be established (severe refractory cases). 17 National Institute for Health and Care Excellence (2005) Obsessive-compulsive disorder and body dysmorphic disorder: treatment. Clinical guideline [CG31]. M https://www.nice.org.uk/guidance/ CG31/chapter/1-Guidance [accessed 20 June 2018]. 18 British Association for Psychopharmacology Guidelines (2014) M https://www.bap.org.uk/ pdfs/BAP_Guidelines-Anxiety.pdf [accessed 20 June 2018]. 19 That is roughly the equivalent of five cups of instant coffee, three cups of freshly brewed coffee, six cups of tea, seven cans of Diet Coke, or six plain chocolate bars, i.e. some patients may already be augmenting themselves!

Obsessive–compulsive disorder 2—management Course Often sudden onset (after stressful event, e.g. loss, pregnancy, sexual problem); presentation may be delayed by 5–10yrs due to secrecy; symptom intensity may fluctuate (contact-related/phasic) or be chronic. Outcome Twenty to 30% significantly improve; 40–50% show moderate improve ment, but 20–40% have chronic or worsening symptoms. Relapse rates are high after stopping medication. Suicide rates i, esp. if there is secondary depression. Prognostic factors • Poor prognosis: giving in to compulsions, longer duration, early onset, ♂, presence of tics, bizarre compulsions, hoarding, symmetry, comorbid depression, delusional beliefs or over-valued ideas, personality disorder (esp. schizotypal). • Better prognosis: good premorbid social and occupational adjustment, a precipitating event, episodic symptoms, less avoidance.

388 Chapter 8 Anxiety and stress-related disorders Olfactory reference disorder Essence Also known as olfactory reference syndrome (ORS), characterized by the erroneous belief that one emits a foul or unpleasant body odour, re sulting in significant distress and impairment, including avoidance of social situations.20 Often accompanied by referential thinking and repetitive be haviours (showering, use of excessive deodorants or perfumes). Level of insight varies, and concerns may amount to having a delusional quality. Differential diagnosis General medical conditions—with verifiable body odour [e.g. hyperhidrosis, halitosis, dental (abscess), trimethylaminuria, rectal abscess/fistulae], (rare) causes of olfactory hallucinations [head injury, migraine, substance use, or seizure disorders—TLE associated with medial temporal lobe tumours and mesial temporal sclerosis (smells: ‘rotting’, ‘bad’, ‘burning rubber’, ‘rotting food’)]. Psychiatric conditions—social anxiety disorder, OCD, body dys morphic disorder, delusional disorder, schizophrenia, schizoaffective dis order, avoidant personality disorder, depression, culture-bound variants [e.g. ‘jikoshu-kyofu’ (Japan); E Culture-bound syndromes?, p. 988]. Comorbidity Depression (usually secondary and may be severe), social anxiety, OCD, body dysmorphic disorder. Epidemiology Prevalence 0.5–2% (estimated) but may be higher as under-reported. Course Onset usually mid-20s but can present earlier at puberty/adolescence, and runs a chronic course. Up to two-thirds may respond to treatments. Treatment Combined approach best. Actively treat any

comorbidity. • Pharmacological—no RCTs; case reports support use of SSRIs (fluoxetine, paroxetine, citalopram, sertraline) or antipsychotics (sulpiride, amisulpride, risperidone, aripiprazole, olanzapine), alone or combined. • Psychological—no RCTs; sparse evidence supports: CBT focusing on compulsive behaviours, low mood, and social avoidance; eye movement desensitization and reprocessing (EMDR) aimed at processing the life events theorized to have been causal in either triggering or maintaining the pathology. 20 The first published descriptions of olfactory reference disorder (ORD) date back to the late 1800s. Also known as autodysomophobia and bromosis, the term ORD was first used in 1971 by Pryse-Phillips to describe the consistent phenomenology observed in a large patient case series of 137 patients (Acta Psychiatr Scand 47:484–509). The world literature has been comprehensively re viewed by Begum and McKenna in 2011 (Psychol Med 41:453–61). Not included in the DSM-5, ORD is being considered for inclusion in ICD-11 as an OCRD.

Hoarding disorder (DSM-5) Hoarding disorder (DSM-5) Essence Persistent difficulties discarding or parting with possessions (including pets), regardless of their actual value, which leads to distress associated with discarding them and results in the accumulation of possessions that clutter active living areas.21 There is significant impairment of social, occupational, and other areas of functioning. Associated with or without excessive acqui sition and varying degrees of insight. Differential diagnosis OCD (obsessions), depressive disorder (poor motivation), psychosis (de lusions), autism (restricted interests), cognitive deficits (dementia, brain in jury, cerebrovascular disease, Prader–Willi syndrome). Comorbidity 75% comorbid mood or anxiety disorder (50% depression, 20% OCD, so cial phobia, and GAD). Epidemiology Prevalence 2–6% in the USA and Europe. More ♂ than ♀ in general popu lation, vice versa in clinical populations. Almost three times more prevalent in older adults (aged 55–94yrs) than younger adults (aged 34–44yrs). Risk factors include: indecisiveness in individuals with the disorder and first- degree relatives; stressful or traumatic life events. Genetic studies suggest 750% of the variability in hoarding disorder is heritable. Course Symptoms may first emerge around ages of 11–15yrs, start interfering with everyday functioning by mid-20s, and cause clinically significant impairment by mid-30s. Usually runs a chronic course. Treatment CBT has some utility, including relaxation, and helps with decision-making and coping skills. Individual, group, or family approaches have been used. Psychotherapy may be augmented with a trial of an SSRI. Actively treat any comorbidity. 21 Also known as Diogenes syndrome (E Personality problems, p. 555)—coined by Clark et al. (1975) but first described by MacMillan and Shaw (1966), the name derives from Diogenes of Sinope, an ancient Greek philosopher, a Cynic who allegedly lived in a large jar in Athens. It is a misnomer as Diogenes was not a hoarder and was known to venture out each day to the Agora. Other suggested synonyms include ‘senile breakdown’, ‘Plyushkin’s syndrome’ (after a character from Gogol’s Dead Souls), ‘social breakdown’, and ‘senile squalor syndrome’.

390 Chapter 8 Anxiety and stress-related disorders Exceptional stressors and traumatic events ICD-10 definition ‘Common sense’ approach: ‘a stressful event or situation . . . of an excep tionally threatening or catastrophic nature, which is likely to cause pervasive distress in almost anyone’. Includes traumatic events (e.g. rape, bombing, criminal assault, natural catastrophe) and unusual sudden changes in the so cial position and/or network of the individual (e.g. domestic fire, multiple bereavement). DSM-5 definition Exposure to actual or threatened death, serious injury, or sexual violence in one (or more) of the following ways: directly experienced, witnessed in person, learning that the traumatic event(s) occurred to a close family member or close friend, or repeated or

extreme exposure to aversive de tails of the traumatic event(s) (e.g. first responders collecting human re mains, police officers repeatedly exposed to details of child abuse). Types I and II trauma (See Box 8.9.) • Type I trauma: single, dangerous, and overwhelming events, comprising isolated (often rare) traumatic experiences of a sudden, surprising, devastating nature, with limited duration (i.e. ICD-10/DSM-5 definitions). • Type II trauma: due to sustained and repeated ordeal stressors (series of traumatic events or exposure to prolonged trauma); may be variable, multiple, chronic, repeated, and anticipated, usually of intentional human design (e.g. ongoing physical or sexual abuse, combat). May lead to 'complex PTSD' or 'complex trauma'. Symptoms include: somatization, dissociation, detachment from others, restricted range or dysregulation of affect, emotional lability (poor impulse-control, self-destructive behaviour, pathological patterns of relationships), and emotional numbing. ICD-10 acknowledges this type of reaction with the diagnosis 'enduring personality changes after catastrophic experience', whereas DSM- 5 allows for coding under 'other specified trauma- and stressor-related disorder' or 'other specified personality disorder'. How common are these events? Community studies have found that up to 80% of men and 75% of women22 experience at least one traumatic event in their lifetime (but see cautionary notes in Box 8.10). Common events include sudden death of a loved one, accidents, fire, flood, natural disasters, or being a witness to severe injury (or murder). 22 Stein MB, Walker JR, Hazen AL, et al. (1997) Full and partial posttraumatic stress disorder: find ings from a community survey. Am J Psychol 154:1114–19.

Exceptional stressors and traumatic events Box 8.9 Continued debate • Both of the ICD-10 and DSM-5 definitions fail to address 'low- magnitude stressors' (e.g. divorce, job loss, failing exams), even though 0.4% of the population may develop 'PTSD-like' symptoms.1 • Equally, 'common' events (e.g. RTAs, sexual assault) quite often lead to PTSD-like symptoms. • Even perpetrators (albeit 'unwilling') of traumatic events (e.g. war-related crimes, torture) may experience PTSD-like symptoms (associated with feelings of shame or guilt). • Emphasis on life-threatening events/threats to physical integrity may also be too restrictive. The perception of threat to, or loss of, autonomy and mental defeat may actually be more significant than physical assault—seen in studies of victims of sexual/physical assault and political prisoners. • Whether diagnosis should be made on the basis of symptom clusters, rather than any definition of what constitutes a 'valid' traumatic event, becomes academic when a patient presents with clinically significant problems (although it may generate much heat when issues of compensation are involved). 1 McNally RJ (2000) Post traumatic stress disorder. In: Millon T, Blaney PH, David RD (eds). Oxford Textbook of Psychopathology, pp. 144–65. Oxford: Oxford University Press. Box 8.10 Recovered and false memories • Survivors of traumatic events, esp. child abuse, sometimes claim to have recovered memories after a long period of time. • Organizations such as the False Memory Syndrome Foundation (USA) and the False Memory Society (UK) suggest that many, if not all, of these recovered memories are the product of inappropriate therapeutic suggestion. • The possibility of false accusations of supposed perpetrators, disruption of families, and accusations of malpractice against therapists have meant that debate is polarized, and subsequently, the literature is very difficult to interpret. • Few would disagree with Lindsay and Read's summary (1995):1 'In our reading, the scientific evidence has clear implications . . . memories recovered via suggestive memory work by people who initially denied any such history should be viewed with skepticism, but there are few grounds to doubt spontaneously recovered memories of common forms of child sexual abuse or recovered memories of details of never-forgotten abuse. Between these extremes lies a grey area within which the implications of existing scientific evidence are less

clear and experts are likely to disagree.’ 1 Lindsay DS, Read JD (1995) ‘Memory work’ and recovered memories of childhood sexual abuse: scientific evidence and public, professional and personal issues. Psychol Publ Policy Law 1:846–908.

392 Chapter 8 Anxiety and stress-related disorders Acute stress reaction (ICD-10) Essence A transient disorder (lasting hours or days) that may occur in an individual as an immediate (within 1hr) response to exceptional stress (e.g. natural ca tastrophe, major accident, serious assault, warfare, rape, multiple bereave ment, fire). The stressor usually involves severe threat to the security or physical integrity of the individual or of a loved person(s). Symptoms/signs Symptoms tend to be mixed/changeable, with an initial state of daze, fol lowed by depression, anxiety (as for GAD; E Generalized anxiety disorder 1—clinical features and aetiology, p. 380), anger, or despair. Presence of social withdrawal, narrowed attention, disorientation, aggression, hopeless ness, over-activity, or excessive grief defines mild (none of these symptoms present), moderate (two present), or severe (four present, or dissociative stupor) forms. Epidemiology Incidence variable across studies, but estimated around 15–20% of individ uals, following exceptional stress. Aetiology No specific theories, as it is a transient disorder. Risk factors Physical exhaustion, presence of other organic factors, elderly. Differential diagnosis PTSD (‘exceptional trauma’, delayed or persistent symptoms, re- experiencing of the traumatic event), adjustment disorder (not necessarily exceptional stressor, wider range of symptoms), concussion/mild brain in jury (neuropsychological testing cannot always distinguish), brief psychotic disorder, dissociative disorders (no clear stressor), substance misuse. Management By definition, no specific treatment needed. Ensure other needs are ad dressed, i.e. safety, security, practical assistance, social supports. Outcome • Once the stressor is removed, symptoms resolve (usually) within a few hours. • If the stress continues, the symptoms tend to diminish after 24–48hrs and are minimal within about 3 days.

Acute stress reaction (ICD-10) 393

394 Chapter 8 Anxiety and stress-related disorders Acute stress disorder (DSM-5) Essence Clear overlap with ‘acute stress reaction’ (symptoms of dissociation, anx iety, hyperarousal), but greater emphasis on dissociative symptoms; onset within 4wks, lasting 3 days to 4wks (after which diagnosis changes to PTSD). Symptoms/signs Similar to PTSD with symptoms in the categories of: re-experiencing of events (intrusion), avoidance, negative mood, and hyperarousal (but lasting no more than 4wks). Also it must be specified whether qualifying traumatic events were experienced directly, witnessed, or indirectly. Epidemiology Incidence depends on trauma, e.g. 13–14% in road traffic accident (RTA) survivors, 19% in victims of assault, 33% in victims of mass shooting. Aetiology Similar to PTSD. • Psychological: ‘re-experiencing symptoms’. Fear response to harmless situations associated with original trauma, perhaps due to emotional memories (i.e. having personal significance). Remodelling underlying schemas requires holding trauma experiences in ‘active’ memory until the process is complete (working through). Dissociation—a mechanism of avoiding overwhelming emotion (i.e. ‘thinking without feeling’), which, if persistent, delays the process of integration. • Biological: neurophysiological changes leading to permanent neuronal changes as a result of the effects of chronic stress or persistent re- experiencing of the stressful event. Neurotransmitters implicated— cathecholamines, 5-HT, GABA, opioids, and glucocorticoids. Risk factors Previous history of psychiatric disorder, previous traumatic event(s), pre morbid depression, or dissociative symptoms. Comorbidity Similar to PTSD (i.e. depression, substance misuse). Differential diagnosis (See Box 8.11.) PTSD (time frame >4wks’ duration),

adjustment disorder (does not meet criteria for ‘traumatic’ event; E Exceptional stressors and traumatic events, p. 390; wider range of symptoms), concussion/mild brain injury (neuro psychological testing cannot always distinguish), brief psychotic disorder, dissociative disorders (no clear stressor), substance misuse.

Acute stress disorder (DSM-5) Management • Simple practical measures: e.g. support, advice regarding police procedures, insurance claims, dealing with the media, course and prognosis, may be all that is required. • Psychological: • Debriefing—may be useful for certain individuals (needing supportive therapy), but reviews suggest there is little positive benefit of single session debriefing alone and may worsen outcome![23] (See also Box 8.12.) • CBT—brief interventions (education, relaxation, graded in vivo exposure, and cognitive restructuring) may reduce the development of chronic problems/PTSD (not immediate, but ~2wks after the event appears best). • Pharmacological: TCAs, SSRIs, and BDZs may be useful for clinically significant symptoms (evidence lacking). Box 8.11 DSM-5 ‘Trauma- and stressor-related disorders’ and ICD-11 ‘Disorders specifically associated with stress’ This new chapter in DSM-5 (and ICD-11 proposals) attempts to accom modate childhood and adult-onset trauma- and stressor-related disorders together. This means that ‘reactive attachment disorder’ and ‘disinhib ited social engagement’ are included. While these disorders may share aetiological pathways (the result of social neglect), the lack of attach ments seen in reactive attachment disorder is not necessarily found in disinhibited social engagement, which may present very much like ADHD (E Attachment, p. 658). The other disorders included in this category are ‘Acute stress dis order’, ‘Adjustment disorders’, ‘PTSD’, and ‘Other/unspecified trauma- and stressor-related disorders’. Like acute stress disorder, PTSD has four symptom clusters: avoidance, persistent negative alterations in cogni tions and mood, re-experiencing, and alterations in arousal and reactivity (which includes irritable or aggressive behaviour and reckless or self- destructive behaviour). Diagnostic thresholds are lowered to allow the diagnosis in children and adolescents, with separate criteria for children aged 6 or younger. ICD-11 proposes a narrowing of PTSD to three core symptoms: re- experiencing, avoidance, and heightened threat perception. Complex PTSD is added—characterized by severe and pervasive problems in affect regula tion; persistent beliefs about oneself as diminished, defeated, or worthless, accompanied by deep and pervasive feelings of shame, guilt, or failure re lated to the traumatic event; and persistent difficulties in sustaining relation ships and in feeling close to others (with a clear relationship with emotionally unstable personality disorder; E Table 12.1, p. 523). A new category of prolonged grief disorder, with symptoms lasting for at least 6mths, clearly exceeding social, cultural, or religious norms for the individual. 23 Rose SC, Bisson J, Churchill R, Wessely S (2002) Psychological debriefing for preventing post traumatic stress disorder (PTSD). Cochrane Database Syst Rev 2:CD000560.

 Outcome By definition, either self-limiting or continues into PTSD. Box 8.12 Debriefing—more harm than good? Surely it is better to get your emotions out than leave them bottled up? Debriefing, a technique that evolved from military psychiatry, where groups discussed their shared experiences, was used with first re sponders, and then to help victims of trauma. The idea was to prevent PTSD and other psychological problems with an efficient and affordable intervention that often comprised a cathartic retelling of events. In the 1980s and 1990s, counsellors were often among the first to arrive at the scene of a crisis. This vogue for debriefing was challenged when a number of trials of single-session debriefing appeared to show a negative effect. In 1997, Bisson and colleagues conducted a study on burn victims and

found that those who received debriefing were more likely to score highly for symp toms of PTSD, anxiety, and depression 13mths later. Similarly, in 2000, a study by Hobbs and colleagues showed that vehicle accident survivors who received debriefing, when compared to those who were simply assessed, had worse PTSD symptoms at 4mths and when followed up 3yrs later. In 2002, a Cochrane systematic review and meta-analysis con cluded: ‘There is no evidence that single session individual psychological debriefing is a useful treatment for the prevention of post traumatic stress disorder after traumatic incidents. Compulsory debriefing of victims of trauma should cease.’ The controversy that ensued is well summarized in a debate article in the British Journal of Psychiatry in 20031 and highlighted the problems with reliance on evidence-based medicine—that ‘by satisfying the rigorous methodological criteria demanded of level I evidence, many RCTs lose validity and become so divorced from clinical reality that their findings are clinically meaningless.’ (E Trust me, I’m an epidemiologist, p. 30). However, rather than throw the baby out with the bath water, it is now generally agreed that debriefing should be part of a comprehensive, prag matic ‘screen and treat’ package that appropriately assesses psychological and practical support needs, allowing early detection and prompt treat ment of stress- or trauma-related disorders. 1 Wessley S, Deahl M (2003) Psychological debriefing is a waste of time. Br J Psychiatry 183:12–14.

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398 Chapter 8 Anxiety and stress-related disorders Adjustment disorders Adjustment disorders sit uneasily between what are regarded as normal or just ‘problematic’ difficulties and the major psychiatric diagnoses. They must occur within 1 (ICD-10) or 3mths (DSM-5) of a particular psychosocial stressor and should not persist for longer than 6mths after the stressor (or its consequences) is removed (except in the case of ‘prolonged depressive reaction’ in ICD-10). Symptoms are ‘clinically significant’ due to marked distress or impairment of normal functioning, and may be ‘subthreshold’ (due to symptom or duration criteria) manifestations of mood disorders, anxiety disorders, stress-related disorders, somatoform disorders, or con duct disorders. Subclassification • ICD-10: brief depressive reaction (>1mth), prolonged depressive reaction (>6mths, but <2yrs), mixed anxiety and depressive reaction, predominant disturbance of other emotions, predominant disturbance of conduct, mixed disturbance of emotion and conduct, and other specified predominant symptoms. Allows inclusion of bereavement/ grief reactions. • DSM-5: specifiers: with depressed mood, anxiety, mixed anxiety and depressed mood, disturbance of conduct, mixed disturbance of emotions and conduct, and unspecified. Specifically excludes bereavement reactions (E Normal and abnormal grief, p. 400). ‘Acute’ disorders <6mths; ‘chronic’ disorders >6mths. Epidemiology Prevalence in inpatient/outpatient psychiatric populations is conservatively estimated at around 5%. In general hospital settings, it may be as high as 20% (physical illness being the primary stressor for up to 70% of these cases). Aetiology By definition, the problems are caused by an identifiable stressor. Individual predisposition plays a greater role than in other conditions, but symptoms would not have arisen without the stressor. Comorbidity Possibly higher incidence of alcohol-related problems than the general population, but no different from other psychiatric disorders. Differential diagnosis Diagnostic uncertainty may arise if debate surrounds whether the stressor is sufficiently severe to be labelled ‘exceptional’ or ‘traumatic’ (acute stress reaction/disorder or PTSD may be considered). Equally, it may be difficult to determine whether symptoms (e.g. low mood, anxiety, sleep disturb ance, anorexia, lack of energy) are attributable to a medical disorder or are primarily psychiatric in nature. Use of alcohol

and drugs (illicit and pre scribed) may complicate the picture.

Adjustment disorders Management • Psychological: the mainstay of management is essentially supportive psychotherapy to enhance the capacity to cope with a stressor that cannot be reduced or removed, and to establish sufficient support (esp. practical help, e.g. provision of carers/childcare, financial support and benefits, OT assessment, contact with specific support groups) to maximize adaption. Ventilation/verbalization of feelings may be useful in preventing maladaptive behaviours (e.g. social isolation, destructive behaviours, suicidal acts), and understanding the 'meaning' of the stressor to the individual may help correct cognitive distortions. • Pharmacological: the use of antidepressants or anxiolytics/hypnotics may be appropriate where symptoms are persistent and distressing (e.g. prolonged depression/dysphoria) or where psychological interventions have proved unsuccessful. Outcome • 5-yr follow-up suggests recovery in 770% (adolescents: 740%), intervening problems in 710% (adolescents: 715%), and development of major psychiatric problems in 720% (adolescents: 745%). • In adults, further psychiatric problems are usually depression/anxiety or alcohol-related problems. 0 There is a very real risk of suicide and self-harm (esp. in younger popu lations). Additional risk factors include poor psychosocial functioning, pre vious psychiatric problems, personality disorder, substance misuse, and mixed mood/behavioural symptoms. Do not ignore.

400 Chapter 8 Anxiety and stress-related disorders Normal and abnormal grief Controversy surrounds how we should regard normal/abnormal grief, and whether they are distinct from depression or other stress-related disorders.24 It is very common for those suffering bereavement to have depressive symptoms. However, it is less common for people to experi ence a clear depressive episode that requires treatment.25 Normal grief is variable in its intensity and duration. Some commentators regard be reavement as just another stressor and argue that, depending on the phe nomenology, grief may be regarded as an acute stress reaction/disorder, an adjustment disorder, or even a form of PTSD ('traumatic grief '). Just as the former reactive/endogenous debate surrounding depression has led to recommendations that 'clinical' symptoms should be treated, a be reaved person should not be denied effective treatment on the basis of 'understandability', nor should arbitrary time frames [e.g. <4wks (ICD- 10), <2mths (DSM-5)] become more important than assessment of clinical need. Definitions • Bereavement: any loss event, usually the death of someone. • Grief: feelings, thoughts, and behaviour associated with bereavement. • 'Normal'—typical symptoms experienced after bereavement include: disbelief, shock, numbness, and feelings of unreality; anger; feelings of guilt; sadness and tearfulness; preoccupation with the deceased; disturbed sleep and appetite and, occasionally, weight loss; and seeing or hearing the voice of the deceased. Usually these symptoms gradually reduce in intensity, with acceptance of the loss and readjustment. A typical 'grief reaction' lasts up to 12mths (mean 6mths), but cultural differences exist. Intensity of grief is usually greatest for the loss of a child, then spouse or partner, then parent. • 'Abnormal (pathological/morbid/complicated)'—grief reaction that is very intense, prolonged, or delayed (or absent), or where symptoms outside the normal range are seen, e.g. preoccupation with feelings of worthlessness, thoughts of death, excessive guilt, marked slowing of thoughts and movements, a prolonged period of not being able to function normally, hallucinatory experiences (other than the image or voice of the deceased) (see Box 8.13). Risk factors for depression after bereavement History of depression, intense early grief/depressive symptoms, lack of so cial support, little experience of death, 'traumatic'/unexpected death. 24 Stroebe MS, Hanson RO, Stroebe W, et al. (eds) (2007) Handbook of Bereavement Research and Practice: 21st

Century Perspectives. Washington, DC: American Psychological Association Press. 25 Results vary, e.g. in one study 16% of late-life widows had depression 13mths after bereavement. Zisook S, Paulus M, Shuchter SR, Judd LL (1997) The many faces of depression following spousal bereavement. J Affect Disord 45:85–95.

Normal and abnormal grief Management Generally ‘normal’ grief does not require specific treatment, although BDZs may be used to reduce severe autonomic arousal or treat problematic sleep disturbance in the short term. Where there are features of ‘abnormal’ grief, or where there are clinical symptoms of depression/anxiety, treatment with antidepressants ought to be considered, along with culturally appro priate supportive counselling (e.g. through organizations such as CRUSE). ‘Near the end of his life Sigmund Freud was consulted by a woman who had become depressed following the death of her husband. After listening to her, Freud quietly stated, “Madam, you do not have a neurosis, you have a misfortune”.’ Wahl CW (1970) Arch Found Thanatol 1: 137. ‘I know of only one functional psychiatric disorder, whose cause is known, whose features are distinctive, and whose course is usually predictable, and this is grief, the reaction to loss. Yet this condition has been so neglected by psychiatrists that until recently it was not even mentioned in the indexes of most of the best-known general textbooks of psychiatry.’ Parkes CM (1986) Bereavement studies of grief in adult life. 2nd edn. Tavistock Publications, London and New York. Box 8.13 Prolonged grief disorder (PGD) [also known as persistent complex bereavement disorder (DSM-5), complicated grief disorder, and traumatic grief] Prigerson et al.,1 a group of international researchers, have attempted to refine this syndrome for inclusion in DSM-5 (only made it into ‘Other spe cified trauma- and stressor-related disorder’—as a condition for future study) and ICD-11 proposals (successfully as ‘Prolonged grief disorder’), with criteria to identify bereaved persons at heightened risk for enduring distress and dysfunction. Criteria require reactions to a significant loss that involve the experience of yearning (e.g. physical or emotional suf fering as a result of the desired, but unfulfilled, reunion with the deceased) and at least five of the following nine symptoms experienced at least daily or to a disabling degree: • Feeling emotionally numb, stunned, or that life is meaningless. • Experiencing mistrust. • Bitterness over the loss. • Difficulty accepting the loss. • Identity confusion. • Avoidance of the reality of the loss. • Difficulty moving on with life. Symptoms must be present at sufficiently high levels for at least 6mths from the death and be associated with functional impairment. 1 Prigerson HG, Horowitz MJ, Jacobs SC, et al. (2009) Prolonged grief disorder: psychometric validation of criteria proposed for DSM-V and ICD-11. PLoS Med 6:e1000121.

402 Chapter 8 Anxiety and stress-related disorders Post-traumatic stress disorder 1: diagnosis Essence Severe psychological disturbance following a traumatic event (E Excessive stressors and traumatic events, p. 390), characterized by involuntary re- experiencing of elements of the event, with symptoms of hyperarousal, avoidance, and emotional numbing. Symptoms/signs Symptoms arise within 6mths (ICD-10) of the traumatic event (delayed onset in 710% of cases) or are present for at least 1mth, with clinically sig nificant distress or impairment in social, occupational, or other important areas of functioning (DSM-5). Both ICD-10 and DSM-5 include: • Two or more ‘persistent symptoms of increased psychological sensitivity and arousal’ (not present before exposure to the stressor): difficulty falling or staying asleep; irritability or outbursts of anger; reckless or self-destructive behaviour (DSM-5); difficulty in concentrating; hypervigilance; exaggerated startle response. Other ICD-10 criteria • Persistent remembering/‘reliving’ of the stressor in intrusive flashbacks, vivid memories, or recurring dreams; and distress when exposed to circumstances

resembling or associated with the stressor. • Actual/preferred avoidance of circumstances resembling/associated with the stressor (not present before exposure to the stressor). • Inability to recall, either partially or completely, some important aspects or the period of exposure to the stressor. Other DSM-5 criteria (More specific; see Boxes 8.12 and 8.14.) Epidemiology Risk of developing PTSD after a traumatic event: 8–13% for men, 20–30% for women. Lifetime prevalence: around 7.8% (♂:♀ = 1:2). Cultural differ ences exist. Some types of stressor are associated with higher rates (e.g. rape, torture, being a prisoner of war). Aetiology • Psychological/biological (E Acute stress disorder (DSM-5), p. 394). • Neuroimaging: reduced hippocampal volume (may relate to appreciation of safe contexts and explicit memory deficits). Dysfunction of the amygdala, hippocampus, septum, and prefrontal cortex may lead to enhanced fear response. High arousal appears to be mediated by the anterior cingulate, medial prefrontal cortex, and thalamus; dissociation by the parietal, occipital, and temporal cortex. • Genetic: higher concordance rates seen in MZ than DZ twins. Risk factors • Vulnerability factors: low education, lower social class, Afro-Caribbean/ Hispanic, ♀ gender, low self-esteem/neurotic traits, previous (or family)

Post-traumatic stress disorder 1: diagnosis history of psychiatric problems (esp. mood/anxiety disorders), previous traumatic events (including adverse childhood experiences and abuse). • Peri-traumatic factors: trauma severity, perceived life threat, peri- traumatic emotions, peri-traumatic dissociation. • Protective factors: high IQ, higher social class, Caucasian, ♂ gender, psychopathic traits, chance to view the body of a dead person. Comorbidity (may be primary or secondary) Depressive/mood disorders, other anxiety disorders, alcohol and drug misuse disorders, somatization disorders. Differential diagnosis Acute stress reaction/disorder, enduring personality change after a cata strophic event (duration at least 2yrs; E Exceptional stressors and traumatic events, p. 390), adjustment disorder (less severe stressor/dif ferent symptom pattern), other anxiety disorder, depressive/mood dis order, OCD, schizophrenia (or associated psychosis), substance-induced disorders. Box 8.14 Other DSM-5 criteria The traumatic event is persistently re-experienced in one (or more) of the following ways: • Recurrent and intrusive distressing recollections of the event, including images, thoughts, or perceptions (or repetitive play in which themes or aspects of the trauma are expressed in children). • Recurrent distressing dreams of the event (or frightening dreams without recognizable content in children). • Dissociative reactions (e.g. flashbacks)—acting or feeling as if the traumatic event were recurring (or re-enactment in play in children). • Intense psychological distress at exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event. • Marked physiological reactions at exposure to internal or external cues that symbolize or resemble an aspect of the traumatic event. Persistent avoidance of stimuli associated with the trauma (not present before the trauma), as evidenced by: • Efforts to avoid thoughts, feelings, or memories associated with the trauma. • Efforts to avoid external reminders (activities, places, or people) that arouse recollections of the trauma. Negative alterations in cognition and mood associated with the traumatic event(s), as evidenced by two (or more) of: • Inability to recall an important aspect of the trauma. • Persistent exaggerated negative beliefs or expectations about self, others, and the world. • Persistent distorted cognitions. • Persistent negative emotional state. • Markedly diminished interest or participation in significant activities. • Feeling of detachment or estrangement from others. • Persistent inability to experience positive emotions.

404 Chapter 8 Anxiety and stress-related disorders Post-traumatic stress disorder 2: management Psychological Meta-analyses support the superior efficacy of trauma-focused treat ments,26,27 specifically trauma-focused CBT and EMDR. These are recom mended as first-line treatments in all recent guidelines. • CBT: includes elements of—education about PTSD, self-monitoring of symptoms, anxiety management, breathing techniques, imaginal reliving, supported exposure to anxiety-producing stimuli, cognitive restructuring (esp. for complicated trauma), anger management. • EMDR: novel treatment using voluntary multi-saccadic eye movements to reduce anxiety associated with disturbing thoughts and to help process the emotions associated with traumatic experiences (see Box 8.15). • Other psychological treatments: • Psychodynamic therapy—focus on resolving unconscious conflicts provoked by the stressful events, the goal being to understand the meaning of the event in the context of the individual. • Stress management (stress inoculation)—teaching skills to help cope with stress such as relaxation, breathing, thought stopping, assertiveness, positive thinking. • Hypnotherapy—use of focused attention to enhance control over hyperarousal and distress, enabling recollection of traumatic event. Concern over possible induction of dissociative states. • Supportive therapy—non-directive, non-advisory method of exploring thoughts, feelings, and behaviours to reach clearer self-understanding. Pharmacological Medication may be considered when there is severe ongoing threat, if the patient is too distressed or unstable to engage in psychological therapy or fails to respond to an initial psychological approach. Where there is a good treatment response, medication should be continued long term, with trial reduction after 12mths. • SSRIs (e.g. paroxetine 20–40mg/day; sertraline 50–200mg/day) are licensed for PTSD, and their use is supported by a systematic review.28 Other unlicensed possibilities include: venlafaxine, mirtazapine, fluoxetine, escitalopram, and fluvoxamine. Other antidepressants: although unlicensed, there is some evidence for TCAs (e.g. amitriptyline, imipramine); MAOIs (e.g. phenelzine) may also reduce anxiety (over- arousal) and intrusiveness, and improve sleep. 26 National Institute for Health and Care Excellence (2005) Post-traumatic stress disorder: manage ment. Clinical guideline [CG26]. M http://www.nice.org.uk/CG26 [accessed 20 June 2018]. 27 Bisson J, Ehlers A, Matthews R, et al. (2007) Systematic review and meta-analysis of psychological treatments for post-traumatic stress disorder. Br J Psychiatry 190:97–104. 28 Stein DJ, Ipser JC, Seedat S (2006) Pharmacotherapy for posttraumatic stress disorder (PTSD). Cochrane Database Syst Rev 1:CD002795.

Post-traumatic stress disorder 2: management It may be helpful to target specific symptoms: • Sleep disturbance (including nightmares): may be improved by mirtazapine (45mg/day), levomepromazine, prazosin (mean dose 9.5mg/day), or specific hypnotics (e.g. zopiclone, zolpidem). • Anxiety symptoms/hyperarousal: consider use of BDZs (e.g. clonazepam 4–5mg/day), buspirone, antidepressants, propranolol. • Intrusive thoughts/hostility/impulsiveness: some evidence for use of carbamazepine, valproate, topiramate, or lithium. • Psychotic symptoms/severe aggression or agitation: may warrant use of an antipsychotic (some evidence for olanzapine, risperidone, quetiapine, clozapine, aripiprazole). Outcome • 750% will recover within first year, 730% will run a chronic course. • Outcome depends on initial symptom severity. Recovery will be helped by: good social support; lack of negative responses from others; absence of ‘maladaptive’ coping mechanisms (e.g. avoidance, denial, ‘safety behaviours’, not talking about the experience, thought suppression, rumination); no further traumatic life events (secondary problems such as physical health, acquired disability, disfigurement, disrupted relationships, financial worries, and litigation). Box 8.15 EMDR controversy In 1987, Francine Shapiro, a California psychologist in private practice, while walking in the woods, preoccupied with disturbing thoughts, dis covered her

anxiety improved during the walk. She realized that she had been moving her eyes back and forth, from one side of the path to the other, while walking. Shapiro tried out variants of this procedure with her clients and found that they felt better too. Her findings were published in 1989, and EMDR was born. Initially developed to help clients with PTSD and other anxiety dis orders, therapists have since extended EMDR to other conditions, including depression, sexual dysfunction, schizophrenia, eating disorders, and stress associated with illnesses such as cancer. Like other serendip itous discoveries, the claims for EMDR were treated with a healthy dose of scepticism, especially when its proponents tried to explain 'how' it worked, using erroneous theories of memory, right–left brain imbalance, and REM sleep-like processing. It became associated with alternative ther apies, such as Roger Callahan's thought field therapy and Gary Craig's emotional freedom therapy. These therapies have all the hallmarks of pseudoscience (E Psychomythology, p. 24). Although the mechanism of action of EMDR is not fully understood, it has been shown that the eye movements are not a necessary component of the therapy. In fact, well- established psychological principles of attention, imaginal exposure, and methods of relaxation are probably sufficient to explain the efficacy of the EMDR procedure. Shapiro F (1995) Eye Movement Desensitization and Reprocessing: Basic Principles, Protocols, and Procedures. New York, NY: Guildford Press.

406 Chapter 8 Anxiety and stress-related disorders Depersonalization (derealization) syndrome Essence A rare disorder, characterized by persistent or recurrent episodes of a distressing feeling of unreality or detachment in relation to the outside world (derealization) or the person's own body, thoughts, feelings, or be haviour (depersonalization). It is viewed as an anxiety-/stress-related dis order in ICD-10, and as one of the 'dissociative disorders' in DSM-5, along with dissociative amnesia, identity disorder, and fugue (E Dissociative (conversion) disorders, p. 868).29 Clinical features Patients may find it difficult to describe their experiences, often reporting feeling 'as if' they are a passive observer of what is going on around them or their own actions. This may be accompanied by an emotional numbness (in ability to experience feelings) and a dream- or trance-like state. There may also be the experience of alterations in the perception of objects or people, appearing unfamiliar or different in respect to the usual colour, shape, dis tance, or size. Insight tends to be preserved (unlike 'passivity phenomena' in psychoses)—the patient recognizes the experiences as abnormal, un pleasant, distressing, and anxiety-provoking. Epidemiology Up to 50% of 'normal' individuals may experience depersonalization in their lifetime (usually in the context of psychological distress), with 1– 2% having more chronic symptoms. In psychiatric populations, it is a very common experience (lifetime prevalence 780%), with persistent symp toms (and associated functional impairment) in 712%. In clinical popu lations: ♂:♀ = 1:2, whereas in the general population: ♂ = ♀. Age of onset usually adolescence/early adulthood (may go undetected in children). Aetiology • Psychoanalytical: ego defence against painful and conflicting memories, impulses, or affects; usually rooted in childhood trauma.30 • Psychological: adaptive response to overwhelming stress, allowing continued function by protecting against potentially overwhelming anxiety. Specific precipitant(s) may not be readily identifiable. 29 ICD-11 'dissociative disorders' proposals include depersonalization–derealization disorder, dis sociative neurological symptom disorder (conversion disorders), dissociative amnesia, trance dis order, possession trance disorder, dissociative identity disorder, and partial dissociative identity disorder. 30 Dangers of attributing present psychopathology to childhood events cannot be overstated, illus trated by high-profile cases of alleged 'recovered memories' (see Box.8.10). Unsubstantiated claims of childhood (or other) abuse should be regarded with caution, and the significance of childhood trauma, even in empirical studies, finds little support. See Pope HG (1997) Psychology

Astray: Fallacies in Studies of ‘Repressed Memory’ and Childhood Trauma. Boca Raton, FL: Upton.

Depersonalization (derealization) syndrome • Biological:31 altered function in systems central to integrated processing of information in the brain (with functional localization in the parietotemporal and limbic areas) where serotonergic mechanisms play a key role. Possible role for the effects of illicit drugs, as 10–20% of patients describe symptoms first occurring when using drugs (esp. cannabis). Comorbidity Anxiety disorders (particularly phobias, panic disorder, OCD), depressive disorders, personality disorders [anankastic/obsessional, borderline per sonality disorder (BPD)]. Differential diagnosis Depersonalization may be experienced in the context of sleep or sensory deprivation, being in unfamiliar surroundings, or an acutely stressful/trau matic situation. May also be a symptom in schizophrenia/psychosis (usually accompanied by a delusional explanation, e.g. Cotard delusion), mood/anx iety disorders, acute intoxication/withdrawal from alcohol, illicit substances (particularly cannabis or hallucinogens), or medication, and in organic dis orders (e.g. hyperventilation, hypoglycaemia, migraine, epilepsy—brief stereotyped episodes, other neurological conditions). Management • Use of rating scales32 (e.g. the Cambridge Depersonalization Scale)33 may assist the assessment of treatment response. • Exclude organic causes with appropriate investigations, which may sometimes include brain imaging (CT/MRI) and EEG. • Comorbid psychiatric conditions should be identified and treated. Despite successful treatment, depersonalization may persist. • Evidence for successful management of depersonalization syndrome is poor. No drugs are licensed for use in the UK. • Some evidence supports a role for SSRIs (usually citalopram or escitalopram), alone or in combination with lamotrigine (up to 500mg/ day). • Where there is marked anxiety, clonazepam (0.5–4mg/day) may be useful; anecdotal evidence supports clomipramine (if obsessional symptoms are marked), naltrexone, and bupropion. • CBT is the only psychological treatment shown to be beneficial in an open trial, particularly in tackling anxieties, ruminations, and avoidance behaviours relating to identifiable stressors. • Other psychotherapeutic approaches: acceptance and understanding of symptoms; identification of ‘putative’ defence functions; identifying underlying psychopathology; integration of traumatic experiences. 31 As early as 1935, Mayer-Gross thought psychological explanations to be of ‘limited value’, seeing depersonalization as ‘an unspecific preformed functional response of the brain’. Mayer-Gross W (1935) On depersonalization. Br J Med Psychol XV:103–26. 32 Medford N, Sierra M, Baker D, et al. (2005) Understanding and treating depersonalization dis order. Adv Psychiat Treat 11:92–100. 33 M https://www.docdroid.net/zIAJlG7/cds-state.pdf [accessed 20 June 2018].

408 Chapter 8 Anxiety and stress-related disorders Course • Onset is usually sudden, with symptoms persisting only for a brief period. Gradual onset does occur, and the course is very variable—both episodic and continuous. Occasionally, symptoms may persist for hours, days, weeks, months, or even years (rare). • Resolution tends to be gradual. Recurrent episodes generally occur in the context of recurring (perceived) stressful situations or fatigue. • Chronic fluctuating symptoms may be treatment-resistant.