26.5.11 Schizophrenia 6513 Stephen M. Lawrie

26.5.11 Schizophrenia 6513 Stephen M. Lawrie

26.5.11 Schizophrenia 6513 Anorexia nervosa The course of anorexia nervosa varies greatly. In the early months and years it may be self-limiting; it may require some form of inter- vention; it may evolve into bulimia nervosa, or another eating disorder; or it may persist and become treatment-resistant. It is par- ticularly important to be aware that anorexia nervosa can be life- threatening. It has a standardized mortality ratio of about six, most deaths being a direct result of medical complications related to star- vation, or suicide. Bulimia nervosa Once fully developed, bulimia nervosa tends to be self-perpetuating. It may persist for years or even decades with adverse effects on self- esteem, career, and relationships. It is common for sufferers to delay seeking help due to the shame associated with binge eating, and it is easy for them to keep the problem secret as their eating in public and appearance are both unremarkable. However, treatment—when sought—is usually effective FURTHER READING Fairburn CG (2008). Cognitive behavior therapy and eating disorders. Guilford Press, New York, NY. Lock J, le Grange D (2013). Treatment manual for anorexia nervosa: a family-based approach. Guilford Press, New York, NY. Mehler PS, Krantz MJ, Sachs KV (2015). Treatments of medical complications of anorexia nervosa and bulimia nervosa. J Eating Disord, 3, 15. National Institute for Health and Care Excellence (NICE) (2017). Eating disorders: recognition and treatment. NICE guideline [NG69]. https://www.nice.org.uk/guidance/ng69 Palmer RL (2014). Helping people with eating disorders, 2nd edition. John Wiley and Sons, Chichester. Royal College of Psychiatrists (2014). Report CR189. MARSIPAN: man- agement of really sick patients with anorexia nervosa, 2nd edition. https:// www.rcpsych.ac.uk/usefulresources/publications/collegereports/cr/ cr189.aspx 26.5.11 Schizophrenia Stephen M. Lawrie ESSENTIALS Schizophrenia is typically a severe chronic mental illness with a high morbidity and increased mortality. It has a complex aetiology including a substantial genetic component. Its clinical features include characteristic delusions and hallucinations. There are no diagnostic tests. The differential diagnosis is from manic states, organic brain dis- orders, and substance misuse. Whilst the management is complex, antipsychotic drugs are effective in reducing symptoms. The overall prognosis is poor; many patients live restricted lives and there is a high rate of suicide. However, some patients return to normal functioning. Importantly for physicians, people with schizophrenia die on average 10 years earlier

than the general population, mainly because of car- diac and cerebrovascular disease, which is often inadequately treated. Introduction A psychotic disorder is a mental illness characterized by hallucin- ations and/or delusions. Schizophrenia is a psychosis in which the hallucinations are typically auditory and the delusions often of a bi- zarre nature. The literal translation of schizophrenia from the Greek is ‘split mind’. This refers to a splitting of mental functions, and has nothing to do with a so-called split personality. Box 26.5.10.4 Principal characteristics of enhanced cognitive behaviour therapy (CBT-E) Aims i. To normalize eating habits and, if applicable, restore body weight ii. To correct the mechanisms that have been maintaining the eating disorder iii. To protect against relapse Format One-to-one treatment (although significant others may attend certain sessions if indicated). Number of sessions: • Nonunderweight patients—about 20 hour-long sessions over 20 weeks. Initial sessions twice-weekly. • Underweight patients—Extended to about 40 hour-long sessions over 40 weeks. Initial sessions twice-weekly. Content Personalized to match the processes maintaining the patient’s eating disorder Two versions: • The focused version is the default version and is suitable for most pa- tients. It focuses exclusively on the eating disorder features. • The broad version is designed for a subgroup of patients in whom certain characteristic problems outside the eating disorder are maintaining the condition, namely extreme perfectionism, marked low self-esteem or major interpersonal difficulties. Four stages: • In stage 1, the focus is on gaining an understanding of the eating problem and helping patients modify and stabilize their pattern of eating. There is also emphasis on personalized education and the ad- dressing of concerns about weight. The sessions are twice-weekly. • In stage 2, progress is systematically reviewed and plans are made for the main body of treatment • Stage 3 consists of a run of weekly sessions focused on the processes that are maintaining the patient’s eating problem. Usually this involves addressing concerns about shape and eating; enhancing the ability to deal with day-to-day events and moods; and reducing dietary restraint. • Towards the end of stage 3 and in stage 4, the emphasis shifts onto the future. The focus is on how to deal with setbacks and maintain improvement.

SECTION 26 Psychiatric and drug-related disorders 6514 Aetiology Genetic factors Schizophrenia runs in families, but the monozygotic concordance rate is only 50% (i.e. the environment clearly plays a significant role). Most cases are likely to be multifactorial and polygenic. The Psychiatric Genomics Consortium recently pooled data from more than 36 000 cases and 100 000 controls and found 108 separate gen- etic loci associated with an increased risk, accounting for about 7% of the variance in liability. Each gene, however, only increases the risk by 5% or less (Table 26.5.11.1). Some of the genes implicated include those concerned with the major histocompatibility complex, calcium signalling, glutamatergic, and dopaminergic neurotrans- mission. There are however some rare genetic variants with larger effects: a 22q11.2 micro-deletion sometimes called DiGeorge syn- drome or velo-cardio facial syndrome increases the risk of schizo- phrenia and other severe mental illnesses about 30 times. Recent advances in genetic technology have allowed the identification of other copy number variations which are deletions or additional copies of genes. These are present in 2–3% of people with schizo- phrenia, and in people with autism and intellectual disability. Environmental factors There is an excess of winter births. This may convey risk by infection or poor nutrition. Neurodevelopmental disruptions such as obstetric complications and minor physical anomalies, motor, cognitive, and social difficulties, all increase the risk of subsequent schizophrenia. Urban birth and upbringing, and adversity in childhood, also in- crease the risk. Chronic, regular use of cannabis and stimulants are among the most potent risk factors for precipitating schizophrenia, but the strongest known environmental risk factor is immigration,

possibly related to the perceived threat or lack of support in an alien environment. Stressful life events may precipitate psychosis in those who are predisposed. Stress, including negative ‘expressed emotion’ (criticism, hostility) from relatives, can also cause relapses. Pathophysiology All effective antipsychotic drugs block dopamine (D2) receptors, and the potency with which they do that correlates with the dose required in clinical practice. This provides indirect evidence for the so-called ‘dopamine hypothesis of schizophrenia’ which posits that acute, positive symptoms are caused by increased dopamine turn- over. This hypothesis is supported by strong evidence that dopa- minergic agonists—ephedrine, cocaine, and amphetamine—can cause psychosis. Direct evidence also comes from an impressively consistent literature showing increased radiolabelled dopamine precursor turnover in presynaptic neurons in the striatum. Acute administration of dopamine agonists increases dopamine turnover and positive psychotic symptoms. Cannabis and social stress may also increase the risk of schizophrenia via release of dopamine. There is, however, as much evidence for disruption in glutamate neurotransmission in schizophrenia. A glutamate theory also offers a better account of the cognitive disruption typically seen in schizo- phrenia, including an average 10-point drop in IQ from premorbid levels. It remains unclear just how these neurochemical disruptions re- sult in the mental changes observed, such as delusions and hallu- cinations. The hypotheses include disrupted dopamine signalling making irrelevant stimuli abnormally salient, causing persecutory delusions, and dysconnection in corollary discharges between lan- guage regions of the cortex, causing auditory hallucinations. Epidemiology Schizophrenia has a modal age at onset of 25 years. It is usually asso- ciated with long-term disability. The prevalence is remarkably con- sistent worldwide at approximately 0.5%. This translates to about 300 000 cases in the United Kingdom. Clinical features The diagnostic criteria in DSM-5 are summarized in Table 26.5.11.2. The ICD-10 diagnostic criteria differ in that they continue to stress the particular importance of Schneider’s’ ‘First Rank Symptoms’ (FRSs) in making the diagnosis. FRSs include certain types of audi- tory hallucinations such as hearing one’s own thoughts spoken aloud (‘echo de la pensee’), hearing voices that comment on what one is doing or thinking (in the second person) or arguing about or dis- cussing one in the third person. FRS also include specific delusions; these include the conviction that thoughts from outside are being inserted into one’s head (‘thought insertion’), that thoughts are being withdrawn from one’s head (‘thought withdrawal’) and that one’s thoughts are broadcast to others (‘thought broadcast’), ‘delusions of passivity’ and feelings or volitions or bodily functions which are ex- perienced as imposed by an outside force or agency. The symptoms of schizophrenia may be divided into: • Positive symptoms: these are pathological by their presence; for example, hallucinations, delusions, disorganized speech (aka ‘thought disorder’, such as ‘loosening of associations’ between ideas), and incongruity of affect (inappropriate laughter or tears). Table 26.5.11.1 The main risk factors for schizophrenia Family history c.50 × increased risk in monozygotic twin of person with schizophrenia 10 × increase in other first degree relatives Immigrant status c.5 × increased risk Childhood adversity c.3 × increased risk Cannabis use (regular) c.3 × increased risk
Table 26.5.11.2 Summary of DSM-5 diagnostic criteria for schizophrenia A–E are all required: A. Two or more of: delusions, hallucinations, disorganized speech, grossly disorganized behaviour, negative symptoms, for one month (less if treated) B. Impaired social or occupational functioning C. Illness continuous over at least six months (including acute phase) D. Any mood disorder is only brief or minor E. Not due to drugs of abuse, medication, or medical illness

 These tend to dominate the clinical picture in the acute phase and respond to antipsychotic medication. • Negative symptoms: these are pathological by their

absence; for example, lack of affect, lack of motivation (avolition), poverty of speech (alogia), and social withdrawal. Negative symptoms do not tend to respond to current treatments, are a poor prognostic sign and tend to dominate the clinical picture in chronic cases. Differential diagnosis To make a diagnosis of schizophrenia it is necessary to identify the key features. This may take time and usually requires a collateral history. The main psychiatric differential diagnosis is from the manic phase of bipolar disorder. In manic states the delusions are usually is in keeping with mood (‘mood congruent’) and the mood disturb- ance dominates the clinical picture. The main medical differential diagnosis is from alcohol or illicit drug misuse, and less commonly from organic psychoses resulting from infections condition such as neurosyphilis, temporal lobe epi- lepsy, and head injury. Impaired conscious level and fluctuating con- fusion suggest an organic syndrome. Drug screening, appropriate investigation, and brain scanning should be considered in all new cases of acute psychosis. Clinical investigations Despite notable scientific progress in understanding the genetic aetiology and pathophysiological mechanisms, there is no object- ively measurable diagnostic abnormality; schizophrenia remains diagnosed as a syndrome based on the clinical picture. However, it has been known for years that patients with schizophrenia have large lateral ventricles and reduced brain volumes, especially in frontotemporal regions. Brain imaging technologies and studies have advanced to the point that structural MRI in particular has been found in research settings to provide an early diagnoses with 80–90% overall accuracy, but such methods are not yet ready for routine clinical use. Treatment Principles of management Treatment with antipsychotic drugs is the mainstay of the treat- ment of schizophrenia. They reduce behavioural disturbance within minutes or hours, reduce acute symptoms in days, and reduce the risk of relapse over months and years. The number needed to treat (NNT) for response in each of these situations is approximately three. Consequently antipsychotic drug treatment for schizophrenia is among the most effective interventions in medicine. Antipsychotic drugs also have limitations, however. They are more effective against positive than negative symptoms. They also have unpleasant adverse effects. Some adverse effects such as sedation can be useful in acute psychosis, but weight gain can be major problem in chronic cases. The other major adverse ef- fect is a range of extrapyramidal side effects. Acute dystonia such as oculogyric crises, trismus, and torticollis can occur within minutes or hours and may require parenteral procyclidene or benztropine. Akathisia and parkinsonism may emerge after days or weeks; while they respond to propranolol or anticholinergics, respectively, they are better avoided by prescribing low doses of antipsychotics in the first place. Tardive dyskinesia can emerge after years of treatment, but is becoming less common. This may reflect the increasing use of so-called ‘second generation’ or ‘atyp- ical’ antipsychotic drugs, which cause few extrapyramidal side ef- fects but more weight gain than ‘first generation’ drugs such as chlorpromazine and haloperidol. As efficacy and adverse effects vary from drug to drug (Table 26.5.11.3), fine-tuning of medication type and dose is needed to optimize effectiveness, promote compliance, and reduce adverse effects. Behavioural, psychological, and social interventions are also ef- fective for patients with schizophrenia and are popular with patients and carers, but are inconsistently implemented. Support and illness education can help patients and carers cope with what is usually a chronic illness, and ‘family intervention’ may help to reduce relatives ‘expressed emotion’. Cognitive behavioural treatment (CBT) seems likely to be useful in most phases of the illness, usually in addition to antipsychotic medication, but the evidence base for this remains controversial. Typically, only 10% of people with schizophrenia will sustain long-term competitive employment, but 50% or so can manage with vocational rehabilitation and ‘job coaches’. Both the so-called ‘re- covery movement’, which stresses that patients can lead satisfying Table 26.5.11.3 Commonly used antipsychotic drugs

Type/name of drug Optimal dosea Main side effects Phenothiazines Chlorpromazine Thioridazine Trifluoperazine 400–600 mg/day 400–600 mg/day 5–10 mg/day Sedation Anticholinergic Extrapyramidal Butyrophenones Haloperidol 8–12 mg/day Extrapyramidal Benzamides Sulpiride Pimozide 800–1200 mg/day 8–10 mg/day Minimal Minimal Depot injections Flupentixol decanoate Fluphenazine decanoate Haloperidol decanoate 40 mg every 2 weeks 25 mg every 2 weeks 100 mg monthly Extrapyramidal Extrapyramidal Extrapyramidal Second-generation drugs Risperidone Olanzapine Quetiapine Amisulpiride 4–6 mg/day 10–15 mg/day 300–600 mg/day 800–1200 mg/day Extrapyramidal Weight gain Sedation Agitation Atypical antipsychotic drugs Clozapine 300–600 mg/day Hypersalivation a This dose of chlorpromazine is established from meta-analyses. Others are calculated as chlorpromazine equivalents. These are less certain for depot, second-generation, and atypical drugs.

SECTION 26 Psychiatric and drug-related disorders 6516 and productive lives, and ‘early psychosis services’, offering holistic care packages for those at risk of or in their first episode of psych- osis, have improved the overall outlook for patients with acute and chronic schizophrenia. The stigmatization of patients with schizophrenia, and those who look after them, remains common. The issue of violent behaviour in particular is frequently misrepresented in the media. While there is a slightly increased risk of violence in acute, unmedicated schizo- phrenia, patients are much more likely to be assaulted that to assault others. Mentally ill people commit less than 10% of all homicides; the public are much more likely to be assaulted by family or friends than by strangers with schizophrenia. Acute treatment Patients in an acute episode, especially if it is their first episode or is associated with illicit drug use, may lack insight into their condition. They may then require compulsory treatment using the law. In the United Kingdom, this is usually under the Mental Health Act. Acute behavioural disturbance, such as agitation or aggression may be treated with a combination of haloperidol (5 mg) and lor- azepam (2 mg). The subsequent regular drug treatment should usu- ally be with a low-potency first generation antipsychotic drug such as chlorpromazine (at a dose of 400–600 mg daily), or a second- generation antipsychotic drug such as risperidone (4–6 mg daily) or olanzapine (10–15 mg daily). Most patients will respond to one or other of these. With the reduction in the numbers of psychiatric beds, there is an emphasis on treatment outside of hospital. Community services, ‘crisis teams’ and ‘intensive home treatment teams’ are often, but not always, able to manage patients in their homes with frequent visits for monitoring and support. Maintenance treatment Numerous randomized trials have found that maintenance use of antipsychotic medication reduces relapse rates at over one year com- pared to placebo (drugs 27% vs. placebo 64%; number needed to treat 3). A smaller dose of antipsychotic drug is often sufficient for maintenance and may enhance compliance. Esterified preparations of antipsychotic drugs allow them to be given as slow releasing fat-soluble depot injections every two to four weeks for patients who want that (rather than taking pills every day), or for those who need to be treated against their will. Approximately one-third of patients will not adequately respond to first- or second-line treatments. They should be offered the only truly ‘atypical antipsychotic drug’, clozapine (300–600 mg daily). This works in most patients with such ‘treatment-resistant schizo- phrenia’, but requires regular blood monitoring to reduce the risk of agranulocytosis. Various psychological and social interventions including cogni- tive behavioural treatment, illness education, and family interven- tion can reduce the relapse rate. Members of the multidisciplinary community mental health teams can provide these and other services. For example, community psychiatric nurses can monitor and support patients, give depot injections, and help patients access other services. Social workers can help with benefits and inde- pendent or supported accommodation. Outcome Some people with schizophrenia have manifest difficulties in their

development, but most have had an unremarkable childhood. The first symptoms are usually a prodromal ‘loss of (mental) con- trol’, anxiety, or depression over months or years before the ad- vent of delusions and hallucinations in early adulthood. Major behavioural changes can accompany the development of delu- sions and hallucinations. Relapses and remissions with some re- sidual disability are typical, and complete lasting recovery is rare. Good treatment response is predicted by a good initial response to medication, but most patients will have a relapsing and remitting illness course, with some ongoing negative symptoms, intermittent positive symptoms, social and occupational impairments between episodes. Predictors of outcome Acute onset and good premorbid functioning predict a better prog- nosis. Living in a developing country may be associated with a better overall outcome, possibly because of greater social support. Five to ten per cent (5–10%) of patients with schizophrenia will commit suicide. Medical morbidity Most people with schizophrenia die of heart attacks, cancer, and strokes, and they do so approximately 10–15 years earlier than population average. This shortened life expectancy is attribut- able to both behaviour and circumstance; most patients smoke heavily and many drink to excess. These effects are compounded by poverty and poor diet and inactivity. There is a major med- ical challenge in correcting the current underinvestigation and undertreatment of these serious medical conditions in people with schizophrenia. FURTHER READING Howes OD, Murray RM (2014). Schizophrenia: an integrated socio- developmental-cognitive model. Lancet, 383, 1677–87. Leucht S, et al. (2012). Antipsychotic drugs versus placebo for relapse prevention in schizophrenia: a systematic review and meta-analysis. Lancet, 379, 2063–71. Schizophrenia Working Group of the Psychiatric Genomics Consortium (2014). Biological insights from 108 schizophrenia- associated genetic loci. Nature, 511, 421–7. Turner DT, et al. (2014). Psychological interventions for psychosis: a meta-analysis of comparative outcome studies. Am J Psychiatry, 171, 523–38. Zarogianni E, Moorhead TW, Lawrie SM (2013). Towards the identi- fication of imaging biomarkers in schizophrenia, using multivariate pattern classification at a single-subject level. Neuroimage Clin, 3, 279–89.

Revision #1
Created 2026-01-22 16:43:58 UTC by Omar Ayman
Updated 2026-01-22 16:43:58 UTC by Omar Ayman