12 - Psychiatric Disorders

Chapter 157. Approach to the Patient With Mental Symptoms

Introduction

Patients with mental complaints or concerns or disordered behavior present in a variety of clinical settings, including primary care and emergency treatment centers. Complaints or concerns may be new or a continuation of a history of mental problems. Complaints may be related to coping with a physical condition or be the direct effects of a physical condition. The method of assessment depends on whether the complaints constitute an emergency or are reported in a scheduled visit. In an emergency, a physician may have to focus on more immediate history, symptoms, and behavior to be able to make a management decision. In a scheduled visit, a more thorough assessment is appropriate.

Routine Psychiatric Assessment

Assessment includes a general medical and psychiatric history and a mental status examination.

History

The physician must determine whether the patient can provide a history, ie, whether the patient readily and coherently responds to initial questions. If not, information is sought from family and caregivers. Even when a patient is communicative, close family members, friends, or caseworkers may provide information that the patient has omitted. Receiving information that is not solicited by the physician does not violate patient confidentiality. Previous psychiatric assessments, treatments, and degree of adherence to past treatments are reviewed, and records from such care are obtained as soon as possible.

Conducting an interview hastily and indifferently with closed-ended queries (following a rigid system review) often prevents patients from revealing relevant information. Tracing the history of the presenting illness with open-ended questions, so that patients can tell their story in their own words, takes a similar amount of time and enables patients to describe associated social circumstances and reveal emotional reactions.

The interview should first explore what prompted the need (or desire) for psychiatric assessment (eg, unwanted or unpleasant thoughts, undesirable behavior). The interviewer then attempts to gain a broader perspective on the patient's personality by reviewing significant life events—current and past—and the patient's responses to them (see Table 157-1). Psychiatric, medical, social, and developmental history is also reviewed.

The personality profile that emerges may suggest traits that are adaptive (eg, resilience, conscientiousness) or maladaptive (eg, self-centeredness, dependency, poor tolerance of frustration) and may show the coping mechanisms used (see Table 163-1 on p. 1554). The interview may reveal obsessions (unwanted and distressing thoughts or impulses), compulsions (urges to do irrational or apparently useless acts), and delusions (fixed false beliefs) and may determine whether distress is expressed in physical symptoms (eg, headache, abdominal pain), mental symptoms (eg, phobic behavior, depression), or social behavior (eg, withdrawal, rebelliousness). The patient should also be asked about attitudes regarding psychiatric treatments, including drugs and psychotherapy, so that this information can be incorporated into the treatment plan.

The interviewer should establish whether a physical condition or its treatment is causing or worsening a mental condition (see p. 1487). In addition to having direct effects (eg, symptoms, including mental ones), many physical conditions cause enormous stress and require coping mechanisms to withstand the pressures related to the condition. Most patients with severe physical conditions experience some kind of adjustment disorder, and those with underlying mental disorders may become unstable.

Observation during an interview may provide evidence of mental or physical disorders. Body language may reveal evidence of attitudes and feelings denied by the patient. For example, does the patient fidget or pace back and forth despite denying anxiety? Does the patient seem sad despite denying feelings of

depression? General appearance may provide clues as well. For example, is the patient clean and well-kept? Is a tremor or facial droop present?

Mental Status Examination

A mental status examination uses observation and questions to evaluate several domains

[**Table 157-1.** Areas to Cover in the Initial Psychiatric Assessment]

of mental function, including speech, emotional expression, thinking and perception, and cognitive functions. Brief standardized screening questionnaires are available for assessing certain components of the mental status examination, including those specifically designed to assess orientation and memory. However, screening questionnaires cannot take the place of a broader, more detailed mental status examination (see Sidebar 168-1 on p. 1588).

General appearance should be assessed for unspoken clues to underlying conditions. Patients' appearance can help determine whether they are unable to care for themselves (eg, they appear undernourished, disheveled, or dressed inappropriately for the weather or have significant body odor), are unable or unwilling to comply with social norms (eg, they are garbed in socially inappropriate clothing), or have engaged in substance abuse or attempted self-harm (eg, they have an odor of alcohol, scars suggesting IV drug abuse or self-inflicted injury).

Speech can be assessed by noting spontaneity, syntax, rate, and volume. A patient with depression may speak slowly and softly, whereas a patient with mania may speak rapidly and loudly. Abnormalities such as dysarthrias and aphasias may indicate a physical cause of mental status changes, such as head injury, stroke, brain tumor, or multiple sclerosis.

Emotional expression can be assessed by asking patients to describe their feelings. The patient's tone of voice, posture, hand gestures, and facial expressions are all considered. Mood (emotions patients report) and affect (emotional state interviewer notes) should be assessed.

Thinking and perception can be assessed by noticing not only what is communicated but also how it is communicated. Abnormal content may take the form of delusions (false, fixed beliefs), ideas of reference (notions that everyday occurrences have special meaning or significance personally intended for or directed to the patient), or obsessions. The physician can assess whether ideas seem to be linked and goal-directed and whether transitions from one thought to the next are logical. Psychotic or manic patients may have disorganized thoughts or an abrupt flight of ideas.

Cognitive functions include the patient's level of alertness; attentiveness or concentration; orientation to person, place, and time; memory; abstract reasoning; insight; and judgment. Abnormalities of cognition most often occur with delirium or dementia or with substance abuse or withdrawal but can also occur with depression.

Medical Assessment of the Patient With Mental Symptoms

Medical assessment of patients with mental symptoms seeks to identify 2 things:

• Physical disorders *mimicking* mental disorders

• Physical disorders *accompanying* mental disorders

Numerous physical disorders cause symptoms mimicking specific mental disorders (see Table 157-2). Other physical disorders may not mimic specific mental syndromes but instead change mood and energy.

Many drugs cause mental symptoms; the most common drug causes are

• CNS-active drugs (eg, anticonvulsants, antidepressants, antipsychotics, sedative/hypnotics, stimulants)

• Anticholinergics (eg, antihistamines)

• Corticosteroids

Numerous other therapeutic drugs and drug classes have also been implicated; they include some classes that may not ordinarily be considered (eg, antibiotics, antihypertensives). Drugs of abuse, particularly alcohol, amphetamines, cocaine, hallucinogens, and phencyclidine (PCP), particularly in overdose, are also frequent causes of mental symptoms. Withdrawal from alcohol, barbiturates, or benzodiazepines may cause mental symptoms (eg, anxiety) in addition to symptoms of physical withdrawal.

In addition to the problem of causing mental symptoms, patients with a mental disorder may develop a physical disorder (eg, meningitis, diabetic ketoacidosis) that causes new or worsened mental symptoms. Thus, a clinician should not assume that all mental symptoms in patients with a known mental disorder are due to that disorder. The clinician may need to be proactive in addressing possible physical causes for mental symptoms, especially in patients unable to describe their physical health because they have psychosis or dementia.

Patients presenting for psychiatric care occasionally have undiagnosed physical disorders (including substance abuse, diabetes, and hypothyroidism) that are not the cause of their mental symptoms but nonetheless require evaluation and treatment.

[**Table 157-2.** Selected Mental Symptoms Due to Physical Disorders]

Evaluation

Medical assessment by history, physical examination, and often brain imaging and laboratory testing is required for patients with • New-onset mental symptoms

• Qualitatively different or atypical symptoms (ie, in a patient with a known or stable mental disorder)

• Mental symptoms that begin at an atypical age

The goal is to diagnose underlying and concomitant physical disorders rather than to make a specific psychiatric diagnosis.

History: History of present illness should note the nature of symptoms and their onset, particularly whether onset was sudden or gradual and whether symptoms followed any possible precipitants (eg, trauma, starting or stopping of a drug or abused substance). The clinician should ask whether patients have had previous episodes of similar symptoms, whether a mental disorder has been diagnosed and treated, and, if so, whether patients have stopped taking their drugs.

Review of systems seeks symptoms that suggest possible causes:

• Vomiting, diarrhea, or both: Dehydration, electrolyte disturbance

• Palpitations: Hyperthyroidism, drug effects including withdrawal

• Polyuria and polydipsia: Diabetes mellitus

• Tremors: Parkinson's disease, withdrawal syndromes

• Difficulty walking or speaking: Multiple sclerosis, Parkinson's disease, stroke

• Headache: CNS infection, complex migraine, hemorrhage, mass lesion

• Fever, cough, and dysuria: Systemic infection

• Paresthesias and weakness: Vitamin deficiency, stroke, demyelinating disease

Past medical history should identify known chronic physical disorders that can cause mental symptoms (eg, thyroid, liver, or kidney disease; diabetes; HIV infection). All prescription and OTC drugs should be reviewed, and patients should be queried about any alcohol or illicit substance use (amount and duration). Family history of physical disorders, particularly of thyroid disease and multiple sclerosis, is assessed. Risk factors for infection (eg, unprotected sex, needle sharing, recent hospitalization, residence in a group facility) are noted.

Physical examination: Vital signs are reviewed, particularly for fever, tachypnea, and tachycardia. Mental status is assessed (see p. 1588), particularly for signs of confusion or inattention. A full physical examination is done, although the focus is on signs of infection (eg, meningismus, lung congestion, flank tenderness), the neurologic examination (including gait testing), and funduscopy to detect signs of increased intracranial pressure (eg, papilledema, loss of venous pulsations). Signs of liver disease (eg, jaundice, ascites, spider angiomas) should be noted. The skin is carefully inspected for self-inflicted wounds or other evidence of external trauma (eg, bruising).

Interpretation of findings: Confusion and inattention (reduced clarity of awareness of the environment—see p. 1669), especially if of sudden onset, fluctuating, or both, indicate the presence of a physical disorder. However, the converse is not true (ie, a clear sensorium does not confirm that the cause is a mental disorder). Other findings that suggest a physical cause include

• Abnormal vital signs (eg, fever, tachycardia, tachypnea)

• Meningeal signs

• Abnormalities noted during the neurologic examination

• Disturbance of gait, balance, or both

• Incontinence

Some findings help suggest a specific cause. Dilated pupils (particularly if accompanied by flushed, hot, dry skin) suggest anticholinergic drug effects. Constricted pupils suggest opioid drug effects or pontine hemorrhage. Rotary or vertical nystagmus suggests PCP intoxication, and horizontal nystagmus often accompanies diphenylhydantoin toxicity. A preceding history of relapsing-remitting neurologic symptoms, particularly when a variety of nerves appear to be involved, suggests multiple sclerosis. Stocking-glove paresthesias may indicate thiamin or vitamin B_{12} deficiency. In patients with hallucinations, the type of hallucination is not particularly diagnostic except that command hallucinations or voices commenting on the patient's behavior probably represent a mental disorder.

Symptoms that began shortly after significant trauma or after beginning a new drug may be due to those events. Drug or alcohol abuse may or may not be the cause of mental symptoms; about 40 to 50% of patients with a mental disorder also have substance abuse (dual diagnosis).

Testing: Patients typically should have

• Pulse oximetry

• Fingerstick glucose testing

• Measurement of therapeutic drug levels

If patients with a known mental disorder have an exacerbation of their typical symptoms and they have no medical complaints, a normal sensorium, and a normal physical examination (including vital signs, pulse oximetry, and fingerstick glucose testing), they do not typically require further laboratory testing. Most other patients should have

• Blood alcohol level, urine toxicology screens (which may also be required for inpatient admission at certain psychiatric facilities), and HIV testing

Many clinicians also measure

• Serum electrolytes (including Ca and Mg), BUN, and creatinine

Electrolyte and renal function tests may be diagnostic and help inform subsequent drug management (eg, for drugs that require adjustment in patients with renal insufficiency).

Other tests are commonly done based on specific findings:

• Head CT: Patients with new-onset mental symptoms or with delirium, headache, history of recent trauma, or focal neurologic findings (eg, weakness of an extremity)

• Lumbar puncture: Patients with meningeal signs or with normal head CT findings plus fever, headache, or delirium

• Thyroid function tests: Patients taking lithium, those with symptoms or signs of thyroid disease, and those > 40 yr with new-onset mental symptoms (particularly females or patients with a family history of thyroid disease)

• Chest x-ray, urinalysis and culture, CBC, C-reactive protein, and blood cultures: Patients with fever

• Liver function tests: Patients with symptoms or signs of liver disease, with history of alcohol or drug abuse, or with no obtainable history

Less often, findings may suggest testing for SLE, syphilis, demyelinating disorders, or vitamin B_{12} or thiamin deficiency.

Behavioral Emergencies

Patients who are experiencing severe changes in mood, thoughts, or behavior or severe, potentially life-threatening drug adverse effects need urgent assessment and treatment. Non-specialists are often the first care providers for outpatients and inpatients on medical units, but whenever possible, such cases should also be evaluated by a psychiatrist.

When a patient's mood, thoughts, or behavior is highly unusual or disorganized, assessment must first determine whether the patient is a

• Threat to self

• Threat to others

The threat to self can include inability to care for self (leading to self-neglect) or suicidal behavior (see p. 1579). Self-neglect is a particular concern for patients with psychotic disorders, dementia, or substance abuse because their ability to obtain food, clothing, and appropriate protection from the elements is impaired.

Patients posing a threat to others include those who are actively violent, those who appear belligerent and hostile (ie, potentially violent), and those who do not appear threatening to the examiner and staff members but express intent to harm another person (eg, spouse, neighbor, public figure).

Causes: Aggressive, violent patients are often psychotic and have diagnoses such as polysubstance abuse, schizophrenia, delusional disorder, or acute mania. Other causes include physical disorders that cause acute delirium (see Table 157-2) and intoxication with alcohol or other substances, particularly methamphetamine, cocaine, and sometimes phencyclidine (PCP) and club drugs (eg, MDMA [3,4-

methylenedioxymethamphetamine]).

General Principles

Management typically occurs simultaneously with evaluation, particularly evaluation for a possible physical disorder (see p. 1487); it is a mistake to assume that the cause of abnormal behavior is a mental disorder or intoxication, even in patients who have a known psychiatric diagnosis or an odor of alcohol. Because patients are often unable or unwilling to provide a clear history, other collateral sources of information (eg, family members, friends, caseworkers, medical records) must be identified and consulted immediately.

Actively violent patients must first be restrained by

• Physical means

• Drugs (chemical restraint)

• Both

Such interventions are done to prevent harm to patients and others and to allow evaluation of the cause of the behavior (eg, by taking vital signs and doing blood tests). Close monitoring, sometimes involving constant observation by a trained sitter, is required. Although clinicians must be aware of legal issues regarding involuntary treatment (see Sidebar 157-1 and p. 1492), such issues must not delay potentially lifesaving interventions.

Potentially violent patients require measures to defuse the situation. Measures that may help reduce agitation and aggressiveness include • Moving patients to a calm, quiet environment (eg, a seclusion room, when available)

• Removing objects that could be used to inflict harm to self or others

• Expressing sympathetic concern for patients and their complaints

• Responding in a confident yet supportive manner

Speaking directly—mentioning that patients seem angry or upset, asking them if they intend to hurt someone—acknowledges their feelings and may elicit information; it does not make them more likely to act out.

Counterproductive measures include

• Arguing about the validity of patients' fears and complaints

• Issuing threats (eg, to call police, to commit them)

• Speaking in a condescending manner

• Attempting to deceive patients (eg, hiding drugs in food, promising them they will not be restrained)

Staff and public safety: When hostile, aggressive patients are interviewed, staff safety must be considered. Most hospitals have a policy to search for weapons (manually, with metal detectors, or both) on patients presenting with disordered behavior.

Patients who are hostile but not yet violent typically do not assault staff members randomly; rather, they assault staff members who anger or appear threatening to them. Doors to rooms should be left open and staff members should avoid positioning themselves between patients and the door so that patients do not feel trapped or threatened; it is preferable that patients run out than assault staff members. Staff members may also avoid appearing threatening by sitting on the same level as patients. Staff members

may avoid angering patients by not responding to their hostility in kind, with loud, angry remarks or arguing. If patients nonetheless become increasingly agitated and violence appears impending, staff members should simply leave the room and summon sufficient additional staff to provide a show of force, which sometimes deters patients. Typically, at least 4 or 5 people should be present (some preferably young and male). However, the team should not bring restraints into the room unless they are definitely to be applied; seeing restraints may further agitate patients.

Verbal threats must be taken seriously. In most states, when a patient expresses the intention to harm a particular person, the evaluating physician is required to warn the intended victim and to notify a specified law enforcement agency. Specific requirements vary by state. Typically, state regulations also require reporting of suspected abuse of children, the elderly, and spouses.

Physical Restraints

Use of physical restraints is controversial and should be considered only when other methods have failed and a patient continues to pose a significant risk of harm to self or others. Restraints may be needed to hold the patient long enough to administer drugs, do a complete assessment, or both. Because restraints are applied without the patient's consent, certain legal and ethical issues should be considered (see Sidebar 157-1).

Restraints are used to

• Prevent clear, imminent harm to the patient or others

• Prevent the patient's medical treatment from being significantly disrupted (eg, by pulling out tubes or IVs) when consent to the treatment has been provided

• Prevent damage to physical surroundings, staff members, or other patients

• Prevent a patient who requires involuntary treatment from leaving (when a locked room is unavailable)

Restraints should not be used for

• Punishment

• Convenience of staff members (eg, to prevent wandering)

Caution is required in overtly suicidal patients, who could use the restraint as a suicide device.

Procedure: Restraints should be applied only by staff members adequately trained in correct techniques and in protecting patient rights and safety.

First, adequate staff are assembled in the room, and patients are informed that restraints must be applied. Patients are encouraged to cooperate to avoid a struggle. However, once the clinician has determined that restraints are necessary, there is no negotiation, and patients are told that restraints will be applied whether or not they agree. Some actually understand and appreciate having external limits on their behavior. In preparation for applying restraints, one person is assigned to each extremity and another to the patient's head. Then, each person simultaneously grasps their assigned extremity and places the patient supine on the bed; one physically fit person can typically control a single extremity of even large, violent patients (provided all extremities are grasped at the same time). However, an additional person is needed to apply the restraints. Rarely, upright patients who are extremely combative may first need to be sandwiched between 2 mattresses.

Leather restraints are preferred. One restraint is applied to each ankle and wrist and attached to the bed frame, not the rail. Restraints are not applied around the chest, neck, or head, and gags (eg, to prevent spitting and swearing) are forbidden. Patients who remain combative in restraints (eg, attempting to upset the stretcher, bite, or spit) require chemical restraint.

Complications: Agitated or violent people brought to the hospital by police are almost always in restraints (eg, handcuffs). Occasionally, young, healthy people have died in police restraints before or shortly after hospital arrival. The cause is often unclear but probably involves some combination of overexertion with subsequent metabolic derangement and hyperthermia, drug use, aspiration of stomach contents into the respiratory system, embolism in people left in restraints for a long time, and occasionally serious underlying medical disorders. Death is more likely if people are restrained in the hobble position, with one or both wrists shackled to the ankles behind their back; this type of restraint may cause asphyxia and should be avoided. Because of these complications, violent patients presenting in police custody should be evaluated promptly and thoroughly and not dismissed as mere sociobehavioral problems.

Sidebar 157-1 Regulatory Issues in Use of Physical Restraints in Aggressive, Violent Patients

Use of physical restraints should be considered a last resort, when other steps have not sufficiently controlled aggressive, potentially violent behavior. When restraints are needed for such a situation, they are legal in all states as long as their use is properly ordered and documented in the patient's medical record. Restraints have the advantage of being immediately removable, whereas drugs may alter symptoms enough or in a way that delays assessment.

The Joint Commission on Accreditation of Healthcare Organizations guidelines for use of restraints in the psychiatric setting state that restraints must be applied under the direction of a licensed independent practitioner (LIP). The LIP must assess the patient within the first hour of restraint placement. The order for continued restraint may be written for up to 4 h at a time. The patient must be evaluated by an LIP or registered nurse during the 4-h interval and before further continuation of the restraint order. At 8 h, the LIP must reevaluate the patient in person before continuing the restraint order.

Hospital accreditation standards require that patients in restraints be continuously observed by a trained sitter. Immediately after restraints have been applied, the patient must be monitored for signs of injury; circulation, range of motion, nutrition and hydration, vital signs, hygiene, and elimination are also monitored. Physical and mental comfort and readiness for discontinuation of restraints as appropriate are also assessed. These assessments should be done every 15 min.

Chemical Restraints

Drug therapy, if used, should target control of specific symptoms.

Drugs: Patients can usually be rapidly calmed or tranquilized using

• Benzodiazepines

• Antipsychotics (typically a conventional antipsychotic, but a 2nd-generation drug may be used)

These drugs are better titrated and act more rapidly and reliably when administered IV (see Table 157-3), but IM administration may be necessary when IV access cannot be achieved in struggling patients. Both classes of drug are effective sedatives for agitated, violent patients. Benzodiazepines are probably preferred for stimulant drug overdoses and for alcohol and benzodiazepine drug withdrawal syndromes, and antipsychotics are preferred for clear exacerbations of known mental disorders. Sometimes a combination of both drugs is more effective; when large doses of one drug are required, using another drug class may limit adverse effects.

Adverse effects of benzodiazepines: Parenteral benzodiazepines, particularly in the doses sometimes needed for extremely violent patients, may cause respiratory depression. Airway management with intubation and assisted ventilation may be required. The benzodiazepine antagonist, flumazenil, may be used, but caution is required because if sedation is significantly reversed, the original behavioral problem may reappear.

Benzodiazepines sometimes lead to further disinhibition of behavior.

Adverse effects of antipsychotic drugs: Antipsychotics, particularly dopamine-receptor antagonists, at therapeutic as well as toxic doses, can have acute extrapyramidal adverse effects (see Table 157-4), including acute dystonia and akathisia (an unpleasant sensation of motor restlessness). These adverse effects may be dose dependent and may resolve once the drug is stopped. Several antipsychotics, including thioridazine, haloperidol, olanzapine, risperidone, and ziprasidone, can cause long QT-interval syndrome and ultimately increase the risk of fatal arrhythmias. Neuroleptic malignant syndrome is also a possibility. For other adverse effects, see p. 1562.

Legal Considerations

Patients with severe changes in mood, thoughts, or behavior are usually hospitalized when their condition is likely to deteriorate without psychiatric intervention and when appropriate alternatives are not available.

[**Table 157-3.** Drug Therapy for Agitated or Violent Patients]

[**Table 157-4.** Treatment of Acute Adverse Effects of Antipsychotics]

Consent and involuntary treatment: If patients refuse hospitalization, the physician must decide whether to hold them against their will. Doing so may be necessary to ensure the immediate safety of the patient or of others or to allow completion of an assessment and implementation of treatment. Criteria and procedures for involuntary hospitalization vary by jurisdiction. Usually, temporary restraint requires a physician or psychologist and one additional clinician, family member, or close contact to certify that the patient has a mental disorder, is a danger to self or to others, and refuses voluntary treatment.

Danger to self includes but is not limited to

• Suicidal ideation or attempts

• Failure to attend to basic needs, including nutrition, shelter, and needed drugs

In most jurisdictions, knowledge of intent to commit suicide requires a health care practitioner to act immediately to prevent the suicide, for example, by notifying the police or another responsible agency.

Danger to others includes

• Homicidal intent

• Placing others in peril

• Failing to provide for the needs or safety of dependents because of the mental disorder

Chapter 158. Anxiety Disorders

Introduction

Everyone periodically experiences fear and anxiety. Fear is an emotional, physical, and behavioral response to an immediately recognizable external threat (eg, an intruder, a runaway car). Anxiety is a distressing, unpleasant emotional state of nervousness and uneasiness; its causes are less clear. Anxiety is less tied to the exact timing of a threat; it can be anticipatory before a threat, persist after a threat has passed, or occur without an identifiable threat. Anxiety is often accompanied by physical changes and behaviors similar to those caused by fear.

Some degree of anxiety is adaptive; it can help people prepare, practice, and rehearse so that their functioning is improved and can help them be appropriately cautious in potentially dangerous situations. However, beyond a certain level, anxiety causes dysfunction and undue distress. At this point, it is maladaptive and considered a disorder.

Anxiety occurs in a wide range of physical and mental disorders, but it is the predominant symptom of several. Anxiety disorders are more common than any other class of psychiatric disorder. However, they often are not recognized and consequently not treated. Left untreated, chronic, maladaptive anxiety can contribute to or interfere with treatment of some physical disorders.

Etiology

The causes of anxiety disorders are not fully known, but both mental and physical factors are involved. Many people develop anxiety disorders without any identifiable antecedent triggers. Anxiety can be a response to environmental stressors, such as the ending of a significant relationship or exposure to a life-threatening disaster. Some physical disorders can directly cause anxiety; they include the following:

• Hyperthyroidism

• Pheochromocytoma

• Hyperadrenocorticism

• Heart failure

• Arrhythmias

• Asthma

• COPD

Other physical causes include use of drugs; effects of corticosteroids, cocaine, amphetamines, and even caffeine can mimic anxiety disorders. Withdrawal from alcohol, sedatives, and some illicit drugs can also cause anxiety.

Symptoms and Signs

Anxiety can arise suddenly, as in panic, or gradually over many minutes, hours, or even days. Anxiety may last from a few seconds to years; longer duration is more characteristic of anxiety disorders. Anxiety ranges from barely noticeable qualms to complete panic. The ability to tolerate a given level of anxiety varies from person to person.

Anxiety disorders can be so distressing and disruptive that depression may result. Alternatively, an anxiety disorder and a depressive disorder may coexist, or depression may develop first, with symptoms and signs of an anxiety disorder occurring later.

Diagnosis

• Exclusion of other causes

• Assessment of severity

Deciding when anxiety is so dominant or severe that it constitutes a disorder depends on several variables, and physicians differ at what point they make the diagnosis. Physicians must first use history, physical examination, and appropriate laboratory tests to determine whether anxiety is due to a physical disorder or drug. They must also determine whether anxiety is better accounted for by another mental disorder. An anxiety disorder is present and merits treatment if the following apply:

• Other causes are not identified.

• Anxiety is very distressing.

• Anxiety interferes with functioning.

• Anxiety does not stop spontaneously within a few days.

Diagnosis of a specific anxiety disorder is based on its characteristic symptoms and signs. Clinicians usually use specific criteria of the *Diagnostic and Statistical Manual of Mental Disorders* , Fourth Edition Text Revision (DSM-IV-TR), which describes the specific symptoms and requires exclusion of other causes of symptoms.

A family history of anxiety disorders (except acute and posttraumatic stress disorders) helps in making the diagnosis because some patients appear to inherit a predisposition to the same anxiety disorders that their relatives have, as well as a general susceptibility to other anxiety disorders. However, some patients appear to acquire the same disorders as their relatives through learned behavior.

Treatment

Treatments vary for the different anxiety disorders, but typically involve a combination of psychotherapy and drug treatment. The most common drug classes used are the benzodiazepines and SSRIs.

Generalized Anxiety Disorder

Generalized anxiety disorder (GAD) is characterized by excessive, almost daily anxiety and worry for ≥ 6 mo about many activities or events. The cause is unknown, although it commonly coexists in people who have alcohol abuse, major depression, or panic disorder. Diagnosis is based on history and physical examination. Treatment is psychotherapy, drug therapy, or both.

GAD is common, affecting about 3% of the population within a 1-yr period. Women are twice as likely to be affected as men. The disorder often begins in childhood or adolescence but may begin at any age.

Symptoms and Signs

The focus of the worry is not restricted as it is in other mental disorders (eg, to having a panic attack, being embarrassed in public, or being contaminated); the patient has multiple worries, which often shift over time. Common worries include work and family responsibilities, money, health, safety, car repairs, and chores.

The course is usually fluctuating and chronic, with worsening during stress. Most people with GAD have one or more other comorbid psychiatric disorders, including major depression, specific phobia, social phobia, and panic disorder.

Diagnosis

• Clinical criteria

Diagnosis is clinical based on criteria in the *Diagnostic and Statistical Manual of Mental Disorders* , Fourth Edition Text Revision (see Table 158-1).

Treatment

• Antidepressants and often benzodiazepines

Certain antidepressants, including SSRIs (eg, paroxetine, starting dose of 20 mg po once/day) and serotonin-norepinephrine reuptake inhibitors (eg, venlafaxine extended-release, starting dose of 37.5 mg po once/day) are effective but typically only after being taken for at least a few weeks. Benzodiazepines (anxiolytics—see Table 158-2) in small to moderate doses are also often and more rapidly effective, although sustained use usually causes physical dependence. One strategy involves starting with concomitant use of a benzodiazepine and an antidepressant. Once the antidepressant becomes effective, the benzodiazepine is tapered.

[**Table 158-1.** Diagnosis of Generalized Anxiety Disorder]

Buspirone is also effective; the starting dose is 5 mg po bid or tid. However, buspirone can take at least 2 wk before it begins to help.

Psychotherapy, usually cognitive-behavioral therapy, can be both supportive and problem-focused. Relaxation and biofeedback may be of some help, although few studies have documented their efficacy.

Obsessive-Compulsive Disorder

Obsessive-compulsive disorder (OCD) is characterized by anxiety-provoking ideas, images, or impulses (obsessions) and by urges (compulsions) to do something that will lessen the anxiety. The cause is unknown. Diagnosis is based on history. Treatment consists of psychotherapy, drug therapy, or, especially in severe cases, both.

OCD occurs about equally in men and women and affects about 2% of the population.

Symptoms and Signs

The dominant theme of the obsessive thoughts may be harm, risk, danger, contamination, doubt, loss, or aggression. Typically, affected people feel compelled to perform repetitive, purposeful rituals to balance their obsessions, as in the following:

• Washing to balance contamination

• Checking to balance doubt

• Hoarding to balance loss

• Avoiding people who may provoke them to balance fear of behaving aggressively

Most rituals, such as hand washing or checking locks, are observable, but some rituals, such as repetitive counting or statements muttered under the breath, are not.

At some point, people with OCD recognize that their obsessions do not reflect real risks and that the behaviors they perform to relieve their concern are unrealistic and excessive. Preservation of insight, although sometimes

[**Table 158-2.** Benzodiazepines]

slight, differentiates OCD from psychotic disorders, in which contact with reality is lost.

Because people with this disorder fear embarrassment or stigmatization, they often conceal their obsessions and rituals, on which they may spend several hours each day. Relationships often deteriorate, and performance in school or at work may decline. Depression is a common secondary feature.

Diagnosis

Diagnosis is clinical based on criteria in the *Diagnostic and Statistical Manual of Mental Disorders* , Fourth Edition Text Revision.

Treatment

• Exposure and ritual prevention therapy

• Often antidepressants

Exposure and ritual prevention therapy is effective; its essential element is exposure to situations or people that trigger the anxiety-provoking obsessions and rituals. After exposure, patients forgo rituals, allowing the anxiety triggered by exposure to diminish through habituation. Improvement often continues for years, especially in patients who master the approach and use it even after formal treatment has ended. However, most patients have incomplete responses as they also do to drugs.

Many experts believe that combining psychotherapy and drug therapy is best, especially for severe cases. SSRIs (see p. 1543) and clomipramine (a tricyclic antidepressant with potent serotonergic effects) are effective. For most SSRIs, low doses (eg, fluoxetine 20 mg po once/day, fluvoxamine 100 mg po once/day, sertraline 50 mg po once/day, paroxetine 40 mg po once/day) are often as effective as larger ones.

Panic Attacks and Panic Disorder

A panic attack is the sudden onset of a discrete, brief period of intense discomfort, anxiety, or fear accompanied by somatic or cognitive symptoms. Panic disorder is occurrence of repeated panic attacks typically accompanied by fears about future attacks or changes in behavior to avoid situations that might predispose to attacks. Diagnosis is clinical. Isolated panic attacks may not require treatment. Panic disorder is treated with drug therapy, psychotherapy (eg, exposure therapy, cognitive-behavioral therapy), or both.

Panic attacks are common, affecting as many as 10% of the population in a single year. Most people recover without treatment; a few develop panic disorder. Panic disorder is uncommon, affecting 2 to 3% of the population in a 12-mo period. Panic disorder usually begins in late adolescence or early adulthood and affects women 2 to 3 times more often than men.

Symptoms and Signs

A panic attack involves the sudden onset of at least 4 of the 13 symptoms listed in Table 158-3. Symptoms usually peak within 10 min and dissipate within minutes thereafter, leaving little for a physician to observe. Although uncomfortable—at times extremely so—panic attacks are not medically dangerous.

Panic attacks may occur in any anxiety disorder, usually in situations tied to the core features of the disorder (eg, a person with a phobia of snakes may panic at seeing a snake). In pure panic disorder, however, some of the attacks occur spontaneously.

Most people with panic disorder anticipate and worry about another attack (anticipatory anxiety) and avoid places or situations where they have previously panicked. People with panic disorder often worry that they have a dangerous heart, lung, or brain disorder and repeatedly visit their family physician or an emergency department seeking help. Unfortunately, in these settings, attention is focused on physical

symptoms, and the correct diagnosis often is not made. Many people with panic disorder also have symptoms of major depression.

Diagnosis

Panic disorder is diagnosed after physical disorders that can mimic anxiety are eliminated and symptoms meet diagnostic criteria stipulated in the *Diagnostic and Statistical Manual of Mental Disorders* , Fourth Edition Text Revision (DSM-IV-TR).

[**Table 158-3.** Symptoms of a Panic Attack]

Treatment

• Often antidepressants, benzodiazepines, or both

• Often nondrug measures (eg, exposure therapy, cognitive-behavioral therapy)

Some people recover without treatment, particularly if they continue to confront situations in which attacks have occurred. For others, especially without treatment, panic disorder follows a chronic waxing and waning course.

Patients should be told that treatment usually helps control symptoms. If avoidance behaviors have not developed, reassurance, education about anxiety, and encouragement to continue to return to and remain in places where panic attacks have occurred may be all that is needed. However, with a long-standing disorder that involves frequent attacks and avoidance behaviors, treatment is likely to require drug therapy combined with more intensive psychotherapy.

Many drugs can prevent or greatly reduce anticipatory anxiety, phobic avoidance, and the number and intensity of panic attacks:

• **Antidepressants:** The different classes—SSRIs, serotonin-norepinephrine reuptake inhibitors (SNRIs), serotonin modulators, tricyclics (TCAs), and monoamine oxidase inhibitors (MAOIs)—are similarly effective. However, SSRIs and SNRIs offer a potential advantage of fewer adverse effects in comparison with other antidepressants.

• **Benzodiazepines:** These anxiolytics—(see Table 158-2) work more rapidly than antidepressants but are more likely to cause physical dependence and such adverse effects as somnolence, ataxia, and memory problems.

• **Antidepressants plus benzodiazepines:** These drugs are sometimes used in combination initially; the benzodiazepine is slowly tapered after the antidepressant becomes effective.

Panic attacks often recur when drugs are stopped.

Different forms of psychotherapy are effective. Exposure therapy, in which patients confront their fears, helps diminish the fear and complications caused by fearful avoidance. For example, patients who fear that they will faint during a panic attack are asked to spin in a chair or to hyperventilate until they feel faint, thereby learning that they will not faint during an attack. Cognitive-behavioral therapy involves teaching patients to recognize and control their distorted thinking and false beliefs and to modify their behavior so that it is more adaptive. For example, if patients describe acceleration of their heart rate or shortness of breath in certain situations or places and fear that they are having a heart attack, they are taught the following:

• Not to avoid those situations

• To understand that their worries are unfounded

• To respond instead with slow, controlled breathing or other methods that promote relaxation

Phobic Disorders

Phobic disorders consist of persistent, unreasonable, intense fears (phobias) of situations, circumstances, or objects. The fears provoke anxiety and avoidance. Phobic disorders are classified as general (agoraphobia and social phobia) or specific. The causes of phobias are unknown. Phobic disorders are diagnosed based on history. Treatment for agoraphobia and social phobia is drug therapy, psychotherapy (eg, exposure therapy, cognitive-behavioral therapy), or both. Some phobias, including specific phobias, are treated mainly with exposure therapy.

Symptoms and Signs

Symptoms depend on the type of phobic disorder, which is classified as general (agoraphobia and social phobia) or specific.

Agoraphobia: Agoraphobia is fear of and anticipatory anxiety about being trapped in situations or places without a way to escape easily and without help if intense anxiety develops. The situations are avoided or they may be endured but with substantial anxiety. Agoraphobia can occur alone or as part of panic disorder.

Agoraphobia without panic disorder affects about 4% of women and 2% of men during any 12-mo period. Peak age at onset is the early 20s; first appearance after age 40 is unusual.

Common examples of situations or places that create fear and anxiety include standing in line at a bank or at a supermarket checkout, sitting in the middle of a long row in a theater or classroom, and using public transportation, such as a bus or an airplane. Some people develop agoraphobia after a panic attack in a typical agoraphobic situation. Others simply feel uncomfortable in such a situation and may never or only later have panic attacks there. Agoraphobia often interferes with function and, if severe enough, can cause people to become housebound.

Social phobia (social anxiety disorder): Social phobia is fear of and anxiety about being exposed to certain social or performance situations. These situations are avoided or endured with substantial anxiety. People with social phobia recognize that their fear is unreasonable and excessive.

Social phobia affects about 9% of women and 7% of men during any 12-mo period, but the lifetime prevalence may be at least 13%. Men are more likely than women to have the most severe form of social anxiety, avoidant personality disorder (see p. 1555).

Fear and anxiety in people with social phobia often centers on being embarrassed or humiliated if they fail to meet expectations. Often the concern is that their anxiety will be apparent through sweating, blushing, vomiting, or trembling (sometimes as a quavering voice) or that the ability to keep a train of thought or find words to express themselves will be lost. Usually, the same activity done alone causes no anxiety. Situations in which social phobia is common include public speaking, acting in a theatrical performance, and playing a musical instrument. Other potential situations include eating with others, signing their name before witnesses, or using public bathrooms.

A more generalized type of social phobia causes anxiety in a broad array of social situations.

Specific phobias: A specific phobia is fear of and anxiety about a particular situation or object (see Table 158-4). The situation or object is usually avoided when possible, but if exposure occurs, anxiety quickly develops. The anxiety may intensify to the level of a panic attack. People with specific phobias typically recognize that their fear is unreasonable and excessive.

Specific phobias are the most common anxiety disorders. Among the most frequent are fear of animals (zoophobia), heights (acrophobia), and thunderstorms (astraphobia or brontophobia). Specific phobias affect about 13% of women and 4% of men during any 12-mo period. Some cause little inconvenience —eg, fear of snakes (ophidiophobia) in city dwellers, unless they are asked to hike in an area where

snakes are found. However, other phobias interfere severely with functioning—eg, fear of closed places (claustrophobia), such as elevators, in people who must work on an upper floor of a skyscraper. Phobia of blood (hemophobia), injections (trypanophobia), needles or other sharp objects (belonephobia), or injury (traumatophobia) occurs to some degree in at least 5% of the population. People

[Table 158-4. Some Common Phobias*]

with a phobia of blood, needles, or injury, unlike those with other phobias or anxiety disorders, can actually faint because an excessive vasovagal reflex causes bradycardia and orthostatic hypotension.

Diagnosis

Diagnosis is clinical based on criteria in the *Diagnostic and Statistical Manual of Mental Disorders* , Fourth Edition Text Revision.

Prognosis

If untreated, agoraphobia usually waxes and wanes in severity. Agoraphobia may disappear without formal treatment, possibly because some affected people conduct their own form of exposure therapy. But if agoraphobia interferes with functioning, treatment is needed.

Social phobia is almost always chronic, and treatment is needed.

The prognosis for specific phobias is more variable when untreated because it may be easy to avoid the situation or object that causes fear and anxiety.

Treatment

• Exposure therapy

• For agoraphobia and social phobia, often cognitive-behavioral therapy

• Sometimes limited use of a benzodiazepine or β-blocker

Because many phobic disorders involve avoidance, exposure therapy, a form of psychotherapy, is the treatment of choice. With structure and support from a clinician who prescribes exposure homework, patients seek out, confront, and remain in contact with what they fear and avoid until their anxiety is gradually relieved through a process called habituation. Exposure therapy helps > 90% of those who carry it out faithfully and is almost always the only treatment needed for specific phobias. Cognitive-behavioral therapy is effective for agoraphobia and social phobia. Cognitive-behavioral therapy involves teaching patients to recognize and control their distorted thinking and false beliefs as well as instructing them on exposure therapy. For example, patients who describe acceleration of their heart rate or shortness of breath in certain situations or places learn by being repeatedly exposed to those situations that their worries about having a heart attack are unfounded and are taught to respond instead with slow, controlled breathing or other methods that promote relaxation.

Very short-term therapy with a benzodiazepine (eg, lorazepam 0.5 to 1.0 mg po) or a β-blocker (propranolol is generally preferred—10 to 40 mg po), ideally about 1 to 2 h before the exposure, is occasionally useful when exposure to an object or situation cannot be avoided (eg, when a person who has a phobia of flying must fly on short notice) or when cognitive-behavioral therapy is either unwanted or has not been successful.

Many people with agoraphobia also have panic disorder, and many of them benefit from drug therapy with an SSRI. SSRIs and benzodiazepines are effective for social phobia, but SSRIs are probably preferable in most cases because, unlike benzodiazepines, they are unlikely to interfere with cognitive-behavioral therapy. β-Blockers are useful for phobias related to public performance.

Stress Disorders

Stress disorders include acute stress disorder and posttraumatic stress disorder.

Acute Stress Disorder

Acute stress disorder is a brief period of intrusive recollections occurring within 4 wk of witnessing or experiencing an overwhelming traumatic event.

In acute stress disorder, people have been through a traumatic event, have recurring recollections of the trauma, avoid stimuli that remind them of the trauma, and have increased arousal. Symptoms begin within 4 wk of the traumatic event and last a minimum of 2 days but, unlike posttraumatic stress disorder, last no more than 4 wk. People with this disorder experience dissociative symptoms.

Diagnosis

Diagnosis is based on criteria recommended by the *Diagnostic and Statistical Manual of Mental Disorders*, Fourth Edition Text Revision (see Table 158-5); these criteria include dissociative symptoms.

Treatment

• Nondrug measures

Many people recover once they are removed from the traumatic situation, shown understanding and empathy, and given an opportunity to describe the event and their reaction to it. To prevent or minimize this disorder, some experts recommend systematic debriefing to assist people who were involved in or witnessed a traumatic event as they process what has happened and reflect on its effect. In one approach to debriefing, the event is referred to as the critical incident and the debriefing is referred to as critical incident stress debriefing (CISD). Other experts have expressed concern and some studies show that CISD may be not be as helpful as supportive, empathic interviewing, may be quite distressful for some patients, and may even impede natural recovery.

Drugs to assist sleep may help, but other drugs are generally not indicated.

[**Table 158-5.** Diagnosis of Acute Stress Disorder]

Posttraumatic Stress Disorder

Posttraumatic stress disorder (PTSD) is recurring, intrusive recollections of an overwhelming traumatic event. The pathophysiology of the disorder is incompletely understood. Symptoms also include avoidance of stimuli associated with the traumatic event, nightmares, and flashbacks. Diagnosis is based on history. Treatment consists of exposure therapy and drug therapy.

When terrible things happen, many people are lastingly affected; in some, the effects are so persistent and severe that they are debilitating and constitute a disorder. Generally, events likely to evoke PTSD are those that invoke feelings of fear, helplessness, or horror. These events might include experiencing serious injury or the threat of death or witnessing others being seriously injured, threatened with death, or actually dying. Combat, sexual assault, and natural or man-made disasters are common causes of PTSD.

Lifetime prevalence approaches 8%, with a 12-mo prevalence of about 5%.

Symptoms and Signs

Most commonly, patients have frequent, unwanted memories replaying the triggering event. Nightmares of the event are common. Much rarer are transient waking dissociative states in which events are relived as if happening (flashback), sometimes causing patients to react as if in the original situation (eg, loud noises such as fireworks might trigger a flashback of being in combat, which in turn might cause patients

to seek shelter or prostrate themselves on the ground for protection).

Patients avoid stimuli associated with the trauma and often feel emotionally numb and disinterested in daily activities. Sometimes the onset of symptoms is delayed, occurring many months or even years after the traumatic event. PTSD is considered chronic if present > 3 mo. Depression, other anxiety disorders, and substance abuse are common among patients with chronic PTSD.

In addition to trauma-specific anxiety, patients may experience guilt because of their actions during the event or because they survived when others did not.

Diagnosis

Diagnosis is clinical based on criteria in the *Diagnostic and Statistical Manual of Mental Disorders* , Fourth Edition Text Revision (see Table 158-6).

Treatment

• Exposure therapy or other psychotherapy, including supportive psychotherapy

• SSRI or other drug therapy

If untreated, chronic PTSD often diminishes in severity without disappearing, but some people remain severely impaired. The primary form of psychotherapy used, exposure therapy, involves exposure to situations that the person

[**Table 158-6.** Diagnosis of Posttraumatic Stress Disorder]

avoids because they may trigger recollections of the trauma. Repeated exposure in fantasy to the traumatic experience itself usually lessens distress after some initial increase in discomfort. Stopping certain ritual behaviors, such as excessive washing to feel clean after a sexual assault, also helps.

Drug therapy, particularly with SSRIs (see p. 1543), is effective. Drugs with mood-stabilizing effects, such as valproate, carbamazepine, and topiramate, can help reduce arousal, nightmares, and flashbacks.

Because the anxiety is often intense, supportive psychotherapy plays an important role. Therapists must be openly empathic and sympathetic, recognizing and acknowledging patients' mental pain and the reality of the traumatic events. Therapists must also encourage patients to face the memories through desensitizing exposure and learning techniques to control anxiety. For survivor guilt, psychotherapy aimed at helping patients understand and modify their self-critical and punitive attitudes may be helpful.

Chapter 159. Dissociative Disorders

Introduction

Everyone occasionally experiences a failure in the normal automatic integration of memories, perceptions, identity, and consciousness. For example, people may drive somewhere and then realize that they do not remember many aspects of the drive because they are preoccupied with personal concerns, a program on the radio, or conversation with a passenger. Typically, such a failure, referred to as nonpathologic dissociation, does not disrupt everyday activities.

People with a dissociative disorder may totally forget a series of normal behaviors occupying minutes or hours and may sense missing a period of time in their experience. Dissociation thus disrupts the continuity of self and the recollection of life events. People may experience the following:

• Poorly integrated memory (dissociative amnesia)

• Fragmentation of identity and memory (dissociative fugue or dissociative identity disorder)

• Disruption of experience and self-perception (depersonalization disorder)

Dissociative disorders are usually attributed to overwhelming stress. Such stress may be generated by traumatic events or by intolerable inner conflict.

Depersonalization Disorder

Depersonalization disorder consists of persistent or recurrent feelings of being detached from one's body or mental processes, usually with a feeling of being an outside observer of one's life. The disorder is often triggered by severe stress. Diagnosis is based on symptoms after other possible causes are ruled out. Treatment consists of psychotherapy.

About 20 to 40% of the general population have had a transient experience of depersonalization, frequently occurring in connection with life-threatening danger, acute drug intoxication (marijuana, hallucinogens, ketamine, Ecstasy), sensory deprivation, or sleep deprivation. Depersonalization can also occur as a symptom in many other mental disorders as well as in physical disorders such as seizure disorders (ictal or postictal). When depersonalization occurs independently of other mental or physical disorders and is persistent or recurrent, depersonalization disorder is present. It is estimated to occur in about 2% of the general population.

Symptoms and Signs

Patients feel detached from their body, mind, feelings, or sensations. Most patients also say they feel unreal (derealization), like an automaton, or as if they were in a dream or in some other way detached from the world. Some patients cannot recognize or describe their emotions (alexithymia). Patients may describe themselves as the "walking dead." Symptoms are almost always distressing and, when severe, profoundly intolerable. Anxiety and depression are common.

Symptoms are often chronic; about one third of patients have recurrent episodes, and two thirds have continuous symptoms. Episodic symptoms sometimes become continuous.

Patients often have great difficulty describing their symptoms and may fear or believe they are going crazy. They always retain the knowledge that their unreal experiences are not real but rather are just the way that they feel. This awareness differentiates depersonalization disorder from a psychotic disorder, in which such insight is always lacking.

Diagnosis

• Medical and psychiatric evaluation

Diagnosis is based on symptoms after ruling out physical disorders, ongoing substance abuse, and other mental disorders (especially anxiety, depression, and other dissociative disorders). Initial evaluation should include MRI and EEG to rule out physical causes, particularly if symptoms or progression are atypical. Urine toxicology tests may also be indicated.

Psychologic tests and special structured interviews and questionnaires are helpful.

Prognosis

Patients often improve without intervention. Complete recovery is possible for many patients, especially if symptoms result from treatable or transient stresses or have not been protracted. In others, depersonalization becomes more chronic and refractory.

Even persistent or recurrent depersonalization symptoms may cause only minimal impairment if patients can distract themselves from their subjective sense of self by keeping their mind busy and focusing on other thoughts or activities. Some patients become disabled by the chronic sense of estrangement, by the accompanying anxiety or depression, or both.

Treatment

• Psychotherapy

Treatment must address all stresses associated with onset of the disorder as well as earlier stresses (eg, childhood emotional abuse or neglect), which may have predisposed patients to late onset of depersonalization.

Various psychotherapies (eg, psychodynamic psychotherapy, cognitive-behavioral therapy) are successful for some patients:

• Cognitive techniques can help block obsessive thinking about the unreal state of being.

• Behavioral techniques can help patients engage in tasks that distract them from the depersonalization.

• Grounding techniques use the 5 senses (eg, by playing loud music or placing a piece of ice in the hand) to help patients feel more connected to themselves and the world and more real in the moment.

• Psychodynamic therapy focuses on underlying conflicts that make certain affects intolerable to the self and thus dissociated.

• Moment-to-moment tracking and labeling of affect and dissociation in therapy sessions works well for some patients.

Various drugs have been used, but none have clearly demonstrable efficacy. However, some patients are apparently helped by serotonin reuptake inhibitors, lamotrigine, opioid antagonists, anxiolytics, and stimulants. However, these drugs may largely be targeting other mental disorders (eg, anxiety, depression) that are often associated with or precipitated by depersonalization.

Dissociative Amnesia

Dissociative amnesia is inability to recall important personal information that is too extensive to be explained by normal forgetfulness. Diagnosis is based on history after ruling out other causes of amnesia. Treatment is psychotherapy, sometimes combined with hypnosis or drug-facilitated interviews.

The information lost would normally be part of conscious awareness and would be described as autobiographic memory—eg, the story of one's life: who one is, where one went, to whom one spoke, and what one did, said, thought, experienced, and felt. Although the forgotten information may be inaccessible to consciousness, it sometimes continues to influence behavior.

Dissociative amnesia is likely underdetected. Prevalence, although not well-established, has been estimated at 2 to 6% in the general population. Dissociative amnesia is most commonly diagnosed in young adults. The amnesia appears to be caused by traumatic or stressful experiences endured or witnessed (eg, physical or sexual abuse, rape, combat, abandonment during natural disasters, death of a loved one, financial troubles) or by tremendous internal conflict (eg, turmoil over guilt-ridden impulses, apparently unresolvable interpersonal difficulties, criminal behaviors).

Symptoms and Signs

The main symptom is memory loss, usually of information regarding traumatic or stressful events or entire periods of the patient's life. Characteristically, patients experience one or more episodes in which they forget some or all of the events that occurred during a period of time. These periods, or gaps in memory, may represent only a few hours or can encompass years. Usually, the forgotten period of time is clearly demarcated.

Patients seen shortly after they become amnestic may appear confused. Some are very distressed; others are indifferent. Some, especially if the amnesia is for the remote past, may not even be aware of it, and if they present for psychiatric help, the presenting complaint is often different.

Diagnosis

• Medical and psychiatric examination

Diagnosis requires a medical and psychiatric examination. Initial evaluation should include MRI to rule out structural causes, EEG to rule out a seizure disorder, and blood and urine tests to rule out toxic causes, such as illicit drug use. Psychologic testing can help better characterize the nature of the dissociative experiences.

Prognosis

Most patients recover their missing memories, and amnesia resolves. However, some are never able to reconstruct their missing past. The prognosis is determined mainly by the patient's life circumstances, particularly stresses and conflicts associated with the amnesia, and by the patient's overall mental adjustment.

Treatment

• To recover memory, a supportive environment and sometimes hypnosis or a drug-induced hypnotic state

• Psychotherapy to deal with issues associated with recovered memories

If memory of only a very short time period is lost, supportive treatment is usually adequate, especially if patients have no apparent need to recover the memory of some painful event.

Treatment for more severe memory loss begins with creation of a safe and supportive environment. This measure alone frequently leads to gradual recovery of missing memories. When it does not or when the need to recover memories is urgent, questioning patients while they are under hypnosis or, rarely, in a drug-induced (barbiturate or benzodiazepine) semihypnotic state can be successful. These strategies must be done gently because the traumatic circumstances that stimulated memory loss are likely to be recalled and to be very upsetting. The questioner also must carefully phrase questions so as not to suggest the existence of an event and risk creating a false memory. The accuracy of memories recovered with such strategies can be determined only by external corroboration. However, regardless of the degree of historical accuracy, filling in the gap as much as possible is often therapeutically useful in restoring continuity to the patient's identity and sense of self and in creating a cohesive narrative. Once the amnesia is lifted, treatment helps with the following:

• Giving meaning to the underlying trauma or conflict

• Resolving problems associated with the amnestic episode

• Enabling patients to move on with their life

Dissociative Fugue

Dissociative fugue is one or more episodes of amnesia in which patients cannot recall some or all of their past and either lose their identity or form a new identity. The episodes, called fugues, result from trauma or stress. Dissociative fugue often manifests as sudden, unexpected, purposeful travel away from home. Diagnosis is based on history, after ruling out other causes of amnesia. Treatment consists of psychotherapy, sometimes combined with hypnosis or drug-facilitated interviews.

The incidence of dissociative fugue has been estimated at ≤ 0.2%, but the rate increases in connection with wars, accidents, and natural disasters.

Etiology

Causes are similar to those of dissociative amnesia (see p. 1503), with some additional factors (eg, prolonged and escalating subacute stress, extreme intrapsychic conflict, intense struggle between a wish to escape from one's life as is and a very harsh superego).

Fugues are often mistaken for malingering (see p. 1574) because like malingering, fugues may absolve people of accountability for their actions or of certain responsibilities or remove them from hazardous situations. However, unlike malingering, fugues are spontaneous, unplanned, and not faked. Many fugues appear to represent disguised wish fulfillment, the only permissible means of escape from severe distress, especially for people with a rigid conscience. For example, a financially distressed executive leaves a hectic life and lives as a farm hand in the country. A fugue may also remove the person from an embarrassing situation or intolerable stress or may be related to issues of rejection or separation. For example, the fugue may say, in effect, "I am not the man who found his wife to be unfaithful." Some fugues may be an alternative response to suicidal or homicidal impulses.

About half of people have only one dissociative fugue, and the others have a few episodes over their lifetime. When dissociative fugue recurs more than a few times, people usually have an underlying dissociative identity disorder.

Symptoms and Signs

The length of a fugue may range from hours to months, occasionally longer. During the fugue, people may appear and act normal or be only mildly confused. They may assume a new name and identity and engage in complex social interactions. However, at some point, confusion about the new identity or a return of the original identity may make them aware of amnesia or cause distress. When the fugue ends, shame, discomfort, grief, depression, intense conflict, and suicidal or aggressive impulses may appear —people must deal with what they left behind. Failure to remember events that occurred during the fugue may cause confusion, distress, or even terror. When the fugue ends, many people recall their past identity and life up to fugue onset; however, for some, recalling is a lengthier and more gradual process, and some aspects of their autobiographic past may never be recalled. A very few people remember nothing or almost nothing about their past indefinitely.

Diagnosis

• Clinical evaluation (usually the disorder is diagnosed retrospectively)

A fugue in progress is rarely recognized. It may be suspected when people seem confused about their identity, puzzled about their past, or confrontational when their new identity is challenged. Often, the fugue is not diagnosed until people abruptly return to their pre-fugue identity and are distressed to find themselves in unfamiliar circumstances.

The diagnosis is usually made retrospectively, based on documentation of the circumstances before travel, the travel itself, and the establishment of an alternate life. When clinicians suspect that a fugue is faked, cross-checking information from multiple sources may reveal inconsistencies that preclude the diagnosis.

Prognosis

Most fugues are brief and self-limited. Impairment after the fugue ends is usually mild and short-lived. However, if the fugue was prolonged and complications due to behavior before or during the fugue are significant, people may have considerable difficulties trying to return to their pre-fugue identity—eg, a soldier who returns after a fugue may be charged with desertion, or a person who marries during a fugue may have inadvertently become a bigamist.

Treatment

• During fugue, restoring missing information

• After fugue ends, psychotherapy

Rarely, people are identified while still in a fugue. In such cases, the following are important:

• Recovering information (possibly with help from law enforcement and social services personnel) about their true identity

• Figuring out why it was abandoned

• Facilitating its restoration

Treatment after the fugue ends involves psychotherapy, sometimes combined with hypnosis or drug-facilitated (barbiturate or benzodiazepine) interviews. However, efforts to restore memory of the fugue period are often unsuccessful. Regardless, a psychiatrist can help people explore how they handle the types of situations, conflicts, and affects that precipitated the fugue and thus foster better future adaptations and solutions and help prevent fugue recurrences.

Dissociative Identity Disorder

Dissociative identity disorder, formerly called multiple personality disorder, is characterized by ≥ 2 identities (called alters or self-states) that alternate. The disorder includes inability to recall important personal information relating to some of the identities. The cause is almost invariably overwhelming childhood trauma, and the disorder is best viewed as a developmental disorder in which extreme trauma interferes with formation of a single cohesive identity. Diagnosis is based on history, sometimes with hypnosis or drug-facilitated interviews. Treatment is long-term psychotherapy, sometimes with drug therapy.

What is known by one identity may or may not be known by another. Some identities appear to know and interact with others in an elaborate inner world, and some identities do this more than others. The system must be mapped out by the psychiatrist over time.

This disorder may be present in about 1% of the general population.

Etiology

Dissociative identity disorder is attributed to the interaction of the following:

• Overwhelming stress (typically extreme childhood mistreatment)

• Insufficient nurturing and compassion in response to overwhelmingly hurtful experiences during

childhood

- Dissociative capacity (ability to uncouple one's memories, perceptions, or identity from conscious awareness)

Children are not born with a sense of a unified identity; it develops from many sources and experiences. In overwhelmed children, many parts of what should have blended together remain separate. Chronic and severe abuse (physical, sexual, or emotional) and neglect during childhood are frequently reported by and documented in patients with dissociative identity disorder. Some patients have not been abused but have experienced an important early loss (such as death of a parent), serious medical illness, or other overwhelmingly stressful events.

In contrast to most children who achieve cohesive, complex appreciation of themselves and others, severely mistreated children may go through phases in which different perceptions, memories, and emotions of their life experiences are kept segregated. Such children may over time develop an increasing ability to escape the mistreatment by "going away" or retreating into their own mind. Each developmental phase or traumatic experience may be used to generate a different self-state.

Symptoms and Signs

Several symptoms are characteristic:

- Fluctuating symptom pictures

- Fluctuating levels of function from highly effective to disabled

- Severe headaches or other pains

- Time distortions, time lapses, and amnesia

- Depersonalization and derealization

Depersonalization refers to feeling unreal, removed from one's self, and detached from one's physical and mental processes. Patients feel like an observer of their life, as if they were watching themselves in a movie. Patients may even feel as if transiently they do not inhabit their bodies. Derealization refers to experiencing familiar people and surroundings as if they were unfamiliar, strange, or unreal.

Patients typically lose time; they experience frequent bouts of amnesia after which they may discover objects or samples of handwriting that they cannot account for or recognize. They may also find themselves in different places from where they last remember being and have no idea why or how they got there. They may refer to themselves in the first person plural (we) or in the third person (he, she, they), sometimes without knowing why.

The switching of identities and the amnestic barriers between them frequently result in chaotic lives. Because the identities often interact with each other, patients typically report hearing inner conversations between other personalities, which comment on or address them. Thus, patients may be misdiagnosed with a psychotic disorder. Although these voices are experienced as hallucinations, they have a distinctly different quality from the typical hallucinations of psychotic disorders such as schizophrenia.

Patients often have a remarkable array of symptoms that can resemble those of anxiety disorders, mood disorders, posttraumatic stress disorder, personality disorders, eating disorders, bipolar disorder, schizophrenia, and seizure disorders. Suicidal ideation and attempts are common, as are episodes of self-mutilation. Many patients abuse substances.

Diagnosis

- Detailed interviews, sometimes with hypnosis or facilitated by drugs

Patients typically have been diagnosed with at least 3 different mental disorders and have been treated unsuccessfully. On average, these patients are in the mental health system for about 6 to 8 yr before the disorder is accurately diagnosed. The skepticism of some physicians regarding the validity of dissociative identity disorder can contribute to misdiagnosis.

The diagnosis requires knowledge of and specific questions about dissociative phenomena. Prolonged interviews, hypnosis, or drug-facilitated (barbiturate or benzodiazepine) interviews are sometimes used, and patients may be asked to keep a journal between visits. All of these measures encourage a shift of personality states during the evaluation. The clinician may over time attempt to map out the different self-states and their interrelationships. Specially designed structured interviews and questionnaires can be very helpful, especially for clinicians who have less experience with this disorder.

The clinician may also attempt to directly contact other identities by asking to speak to the part of the mind involved in behaviors for which patients had amnesia or that were experienced in a depersonalized or derealized way.

Prognosis

Symptoms wax and wane spontaneously, but dissociative identity disorder does not resolve spontaneously. Patients can be divided into groups based on their symptoms:

1: Symptoms are mainly dissociative and posttraumatic. These patients generally function well and recover completely with treatment.

2: Dissociative symptoms are combined with prominent symptoms of other disorders, such as personality disorders, mood disorders, eating disorders, and substance abuse disorders. These patients improve more slowly, and treatment may be less successful or longer and more crisis-ridden.

3: Patients not only have severe symptoms due to coexisting mental disorders but may also remain deeply emotionally attached to their abusers. These patients can be challenging to treat, often requiring longer treatments that typically aim to help control symptoms more than to achieve integration.

Treatment

• Supportive care, including drug treatment as needed for associated symptoms

• Long-term integration of identity states when possible

Integration of the identity states is the most desirable outcome. Drugs are widely used to help manage symptoms of depression, anxiety, impulsivity, and substance abuse but do not relieve dissociation per se; treatment to achieve integration centers on psychotherapy. For patients who cannot or will not strive for integration, treatment aims to facilitate cooperation and collaboration among the identities and to reduce symptoms.

The first priority of psychotherapy is to stabilize patients and ensure safety, before evaluating traumatic experiences and exploring problematic identities. Some patients benefit from hospitalization, during which continuous support and monitoring are provided as painful memories are addressed. Hypnosis may help with accessing the identities, facilitating communication between them, and stabilizing and interpreting them. Modified exposure techniques can be used to gradually desensitize patients to traumatic memories, which are sometimes tolerated only in small fragments.

As the reasons for dissociations are addressed and worked through, therapy can move toward reconnecting, integrating, and rehabilitating the patient's alternate selves, relationships, and social functioning. Some integration occurs spontaneously during treatment. Integration can be encouraged by negotiating with and arranging the unification of the identities or facilitated with imagery and hypnotic suggestion.

Chapter 160. Drug Use and Dependence

Introduction

Some people who use drugs use large enough amounts often enough and long enough to become dependent.

Definitions

A single definition for drug dependence is elusive. Concepts that aid in defining drug dependence are tolerance and psychologic and physical dependence.

Tolerance describes the need to progressively increase the drug dose to produce the effect originally achieved with smaller doses.

Psychologic dependence includes feelings of satisfaction and a desire to repeat the drug experience or to avoid the discontent of not having it. This anticipation of effect is a powerful factor in the chronic use of psychoactive drugs and, with some drugs, may be the only obvious reason for intense craving and compulsive use. Craving and compulsion to use a drug lead to using it in larger amounts, more frequently, or over a longer period than was intended when use began. Psychologic dependence involves giving up social, occupational, or recreational activities because of drug use, as well as persistent use despite knowing that the drug is likely causing a physical or mental problem. Drugs that cause psychologic dependence often have ≥ 1 of the following effects:

• Reduced anxiety and tension

• Elation, euphoria, or other pleasurable mood changes

• Feelings of increased mental and physical ability

• Altered sensory perception

• Changes in behavior

Drugs that cause chiefly psychologic dependence include marijuana, amphetamine, 3,4-methylenedioxymethamphetamine (MDMA), and hallucinogens, such as lysergic acid diethylamide (LSD), mescaline, and psilocybin.

Physical dependence is manifested by a withdrawal (abstinence) syndrome, in which untoward physical effects occur when the drug is stopped or when its effect is counteracted by a specific antagonist. Drugs that cause strong physical dependence include heroin, alcohol, benzodiazepines, and cocaine. Abstinence syndromes are drug-specific or drug class-specific and may vary considerably based on the amount and frequency of use and on patient characteristics, which may affect how patients experience withdrawal.

Addiction, a concept without a consistent, universally accepted definition, is used here to refer to compulsive use and overwhelming involvement with a drug, including spending an increasing amount of time obtaining the drug, using the drug, or recovering from its effects. It may occur without physical dependence. Addiction implies the risk of harm and the need to stop drug use, regardless of whether the addict understands and agrees.

Drug abuse is definable only in terms of societal disapproval. Drug abuse may involve the following:

• Experimental and recreational use of drugs, which is usually illegal

• Unsanctioned or illegal use of psychoactive drugs to relieve problems or symptoms

• Use of drugs because of dependence or the need to prevent withdrawal

Illicit drug use, although usually considered abuse simply because it is illegal, does not always involve dependence. Use of legal substances, such as alcohol and prescription drugs, may involve dependence and abuse. Abuse of prescription and illegal drugs cuts across all socioeconomic groups.

Recreational drug use has increasingly become a part of Western culture, although in general, it is not sanctioned by society. Some users apparently are unharmed; they tend to use drugs episodically in relatively small doses, precluding clinical toxicity and development of tolerance and physical dependence. Many recreational drugs (eg, crude opium, alcohol, marijuana, caffeine, hallucinogenic mushrooms, coca leaf) are "natural" (ie, close to plant origin); they contain a mixture of relatively low concentrations of psychoactive compounds and are not isolated psychoactive compounds. Recreational drugs are most often taken orally or inhaled. Taking these drugs by injection makes it harder to predict and control desired and unwanted effects.

Intoxication refers to development of a reversible substance-specific syndrome of mental and behavioral changes that may involve altered perception, euphoria, cognitive impairment, impaired judgment, impaired physical and social functioning, mood lability, belligerence, or a combination. Taken to the extreme, intoxication can lead to overdose, significant morbidity, and risk of death.

Narcotics and scheduled drugs: Narcotics are drugs that cause insensibility or stupor (narcosis), but the term is typically restricted to drugs that bind to opiate receptors: opium, opium derivatives, and their semisynthetic and synthetic analogues. However, the US government classifies cocaine as a narcotic, even though it does not bind at opiate receptors or have morphine-like effects. Many narcotics (specifically opioids) are used therapeutically to induce anesthesia and to relieve pain, cough, and diarrhea. The morphine-like effects of opioids are welcomed in most clinical situations but contribute to the attractiveness of narcotics for abuse.

In the US, the Comprehensive Drug Abuse Prevention and Control Act of 1970 and subsequent modifications require the pharmaceutical industry to maintain physical security of and strict record keeping for certain classes of drugs (controlled substances—see Table 160-1). Controlled substances are divided into 5 schedules (or classes) on the basis of their potential for abuse, accepted medical use, and accepted safety under medical supervision. The schedule classification determines how a substance must be controlled.

- Schedule I: These substances have a high potential for abuse, no accredited medical use, and a lack of accepted safety. They can be used only under government-approved research conditions.

- Schedule II to IV: Going from schedule II to IV, these drugs have progressively less potential for abuse. They have an accredited medical use. Prescriptions for these drugs must bear the physician's federal Drug Enforcement Administration (DEA) license number.

- Schedule V: These substances are least likely to be abused. Some Schedule V drugs do not require a prescription.

[**Table 160-1.** Some Examples of Controlled Substances]

State schedules may vary from federal schedules.

Drug Dependence

People usually progress from experimentation to occasional use and then to dependence. This progression is complex and only partially understood. The process depends on interaction between the drug, user, and setting.

Drug: Commonly used psychoactive drugs vary in their potential for creating dependence.

User: The user's predisposing physical characteristics (probably including genetic predisposition), personal characteristics, and circumstances (eg, coexistence of other disorders) influence whether drug

dependence develops. For example, sadness, emotional distress that is symptomatically relieved by the drug, and a sense of social alienation may lead to increased use and dependence or addiction. Psychiatric disorders increase the risk of becoming drug dependent.

Patients with chronic pain (eg, back pain, pain due to sickle cell disease, neuropathic pain, fibromyalgia) often require narcotics for relief; many subsequently become dependent, and a few become addicted. However, in many of these patients, nonnarcotic drugs and other treatments (see p. 1629) are not adequate to relieve pain and suffering.

Few differences exist between the biochemical, drug dispositional, and physical responsiveness of people who become addicted or dependent and those who do not, although such differences have been vigorously sought. However, exceptions exist; nonalcoholic relatives of alcoholics have a diminished physical response to alcohol. Consequently, they need to drink more to get the desired effect.

A neural substrate for reinforcement (the tendency to seek more drugs and other stimuli) has been identified in animal models. In these studies, self-administration of such drugs as opioids, cocaine, amphetamine, nicotine, and benzodiazepines is associated with enhanced dopaminergic transmission in specific mid-brain and cortical circuits. This finding suggests the existence of a brain reward pathway involving dopamine in the mammalian brain. However, evidence that hallucinogens and cannabinoids activate this system is insufficient, and not everyone who experiences these rewards becomes dependent or addicted.

An addictive personality has been described variously by behavioral scientists, but little scientific evidence backs this concept.

Setting: Cultural and social factors include peer or group pressure and environmental stress (particularly if accompanied by feelings of impotence to effect change or to accomplish goals).

Physicians may inadvertently contribute to harmful use of psychoactive drugs by overzealously prescribing them to patients for stress relief or may be manipulated by patients to overprescribe the drugs. Many social factors and the mass media may contribute to the expectation that drugs can safely relieve all distress and gratify all needs.

Injection Drug Use

A number of drugs of abuse are given by injection to achieve a more rapid or potent effect or both. Drugs are typically injected IV but may be injected sc, IM, or even sublingually. Users typically access peripheral veins, but when these have sclerosed because of chronic use, some learn to inject into large central veins (eg, internal jugular, femoral, axillary).

Complications

People who inject illicit drugs risk not only the adverse pharmacodynamic effects of the drugs but also complications related to contaminants, adulterants, and infectious agents that may be injected with the drug.

Adulterants: Some drug users crush tablets of prescription drugs, dissolve them, and inject the solution IV, thus injecting themselves with an array of filler agents commonly present in tablets, including cellulose, talc, and cornstarch. Filler agents can become trapped by the pulmonary capillary bed and result in chronic inflammation and foreign body granulomatosis. Filler agents can also damage the endothelium of heart valves, thus increasing the risk of endocarditis.

Street drugs such as heroin and cocaine are often "cut" with various adulterants (eg, amphetamines, clenbuterol, dextromethorphan, fentanyl, ketamine, lidocaine, lysergic acid diethylamide [LSD], pseudoephedrine, quinine, scopolamine, xylazine). Adulterants may be added to enhance mind-altering properties or to substitute for pure drug; their presence can make diagnostic and therapeutic decisions difficult.

Infectious agents: Needle sharing and use of nonsterile techniques can lead to many infectious complications. Injection site complications include cutaneous abscesses, cellulitis, lymphangitis, lymphadenitis, and thrombophlebitis. Distant focal infectious complications due to septic emboli and bacteremia include bacterial endocarditis and abscesses in various organs and sites. Septic lung emboli and osteomyelitis (particularly lumbar vertebral) are particularly common. Infectious spondylitis and sacroiliitis may occur.

Systemic infectious diseases are primarily hepatitis B and C and HIV infection. IV drug users are at high risk of pneumonia, resulting from aspiration or hematogenous spread of bacteria. Other infections that are not directly caused by drug injection but are common among IV drug users include TB, syphilis, and other sexually transmitted diseases. Even botulism and tetanus can result from IV drug abuse.

Diagnosis

• History, physical examination, or both

Some patients readily admit to injection drug use, but for others, a thorough physical examination is needed to detect evidence of injection. Chronic IV drug use can be confirmed by observing track marks due to repeated injections into subcutaneous veins. Track marks are a linear area of tiny, dark punctate lesions (needle punctures) surrounded by an area of darkened or discolored skin due to chronic inflammation. Track marks are often found in easily accessible sites (eg, antecubital fossa, forearms), but some drug users try to hide evidence of their injections by choosing less obvious sites (eg, axillae). Subcutaneous injection (skin popping) can cause characteristic circular scars or ulcers; there may be signs of previous abscesses. Addicts may deny stigmata of drug use by attributing track marks to frequent blood donations, bug bites, or previous trauma.

Treatment

• Prevention and treatment of infectious complications

Drug users, especially those with a history of injection drug use, should be thoroughly evaluated for viral hepatitis, HIV infection, and the wide range of other infectious diseases common among these patients (eg, TB, syphilis, other sexually transmitted diseases). Also, vaccination to prevent hepatitis, influenza, pneumococcal infection, and other infections should be offered to all appropriate patients.

The AIDS epidemic has triggered a harm-reduction movement, which aims to reduce the harm of drug use without necessarily requiring cessation. For example, providing clean needles and syringes for users who cannot stop injecting drugs reduces the spread of HIV and hepatitis.

Treatment of infectious complications is the same as that for similar infections resulting from other conditions; it includes use of antibiotics and incision and drainage of abscesses. Treatment may be complicated by difficulty obtaining venous access (and keeping the patient from using it to inject more drugs) and by poor adherence to treatment regimens.

Drug Testing

Drug testing is done primarily to screen people systematically or randomly for evidence of use of one or more substances with potential for abuse. Testing is done in the following circumstances:

• Certain groups of people, commonly including students, athletes, and prisoners

• People who are applying for or who already hold certain types of jobs (eg, pilots, commercial truck drivers)

• People who have been involved in motor vehicle or boating accidents or accidents at work

• People who have attempted suicide by unclear means

- People in a court-ordered treatment program or with terms of probation or parole requiring abstinence (to monitor adherence)

- People in a substance abuse treatment program (as a standard feature, to obtain objective evidence about substance abuse and thus optimize treatment)

- People required to participate in a drug testing program as part of custody or parental rights

Notification or consent may be a requirement before testing, depending on jurisdiction and circumstances. Mere documentation of use may be sufficient for legal purposes; however, testing cannot determine frequency and intensity of substance use and thus cannot distinguish casual users from those with more serious problems. Also, drug testing targets only a limited number of substances and thus does not identify many others. The clinician must use other measures (eg, thorough history, questionnaires) to identify the degree to which substance use has affected each patient's life.

Alcohol, marijuana, cocaine, natural and semisynthetic opioids, amphetamines, and phencyclidine are the substances most commonly tested for. Testing for benzodiazepines and barbiturates may also be done. Urine, blood, breath, saliva, sweat, or hair samples may be used. Urine testing is most common because it is noninvasive, quick, and able to qualitatively detect a wide range of drugs. The window of detection depends on the frequency and amount of drug intake but is about 1 to 4 days for most drugs. Because cannabinoid metabolites persist, urine tests for marijuana can remain positive longer after use is stopped. Blood testing can be used to quantify levels of certain drugs but is less commonly done because it is invasive and the window of detection for many drugs is much shorter, often only hours. Hair analysis is not as widely available but provides the longest window of detection, ≥ 100 days for some drugs.

Validity of testing depends on the type of test done. Screening tests are typically rapid qualitative urine immunoassays. Such screening tests are associated with a number of false-positive and false-negative results, and they do not detect meperidine and fentanyl. Lysergic acid diethylamide (LSD), gamma hydroxybutyrate (GHB), mescaline, and inhaled hydrocarbons are not detected on readily available screens. Confirmatory tests, which may require several hours, typically use gas chromatography or mass spectroscopy.

False results: Several factors can produce false-negative results, particularly in urine testing. Patients may submit samples provided by others (presumably drug-free). This possibility can be eliminated by directly observing sample collection and by sealing samples immediately with tamper-evident seals. Some people attempt to defeat urine drug testing by drinking large quantities of fluids or by taking diuretics before the test; however, samples that appear too clear can be rejected if specific gravity of the sample is very low.

False positives can result from ingesting prescription and nonprescription therapeutic drugs and from consuming certain foods. Poppy seeds may produce false-positive results for opioids. Pseudoephedrine, tricyclic antidepressants, and quetiapine may produce false-positive results for amphetamines, and ibuprofen may produce false-positive results for marijuana.

Body Packing

Body packing is the voluntary or coerced swallowing of drug-filled packets to smuggle drugs across borders or other security checkpoints.

Body packing often involves drugs with a high street value (primarily heroin or cocaine). The drugs may be placed in condoms or in packets enclosed by several layers of polyethylene or latex and sometimes covered with an outer layer of wax. After body packers ("mules") swallow multiple packets, they typically take antimotility drugs to decrease intestinal motility until the packets can be retrieved. Rupture of one or more packets is a risk, resulting in abrupt toxicity and overdose. Specific symptoms depend on the drug, but intractable seizures, tachycardia, hypertension, and hyperthermia are common with cocaine, and coma and respiratory depression are common with heroin. Intestinal obstruction or rupture and peritonitis are also risks.

Body stuffing is similar to body packing; it occurs when people about to be apprehended by law enforcement swallow drug packets to avoid detection. Sometimes packets are placed in the rectum or vagina. Body stuffing usually involves much smaller amounts of drugs than does body packing, but the drugs are usually less securely wrapped, so overdose is still a concern.

Diagnosis

Suspected body packers are usually brought to medical attention by law enforcement officials, but clinicians should consider body packing if recent travelers and newly incarcerated people present with coma or seizures of unknown etiology. Body packing can sometimes be confirmed when packets are detected during rectal examination. Plain x-rays can often confirm the presence of packets in the GI tract.

Treatment

• Supportive treatment for complications

Treatment of patients with symptoms of overdose (and presumed packet rupture) is supportive and includes airway protection, respiratory and circulatory support, and anticonvulsants, depending on patient symptoms. Sometimes, specific antidotes are indicated (see under specific drugs). Usually, unruptured packets can be removed by whole-bowel irrigation. However, once packets rupture, immediate surgical or endoscopic removal (depending on location in the GI tract) of all packets is indicated but can rarely be done in time; death commonly occurs because the quantity of drug released is large. Patients with intestinal obstruction or perforation also need immediate surgery. Activated charcoal may be helpful but is contraindicated in patients with obstruction or perforation.

Asymptomatic body packers should be observed for development of symptoms until the packets are passed and followed by several packet-free stools. Some clinicians use whole-bowel irrigation with a polyethylene glycol solution with or without metoclopramide as a promotility agent. Emergency endoscopy is not indicated for asymptomatic patients.

Opioids

Opioids are euphoriants that, in high doses, cause sedation and respiratory depression. Respiratory depression can be managed with specific antidotes (eg, naloxone) or with endotracheal intubation and mechanical ventilation. Withdrawal manifests initially as anxiety and drug craving, followed by increased respiratory rate, diaphoresis, yawning, lacrimation, rhinorrhea, mydriasis, and stomach cramps and later by piloerection, tremors, muscle twitches, tachycardia, hypertension, fever, chills, anorexia, nausea, vomiting, and diarrhea. Diagnosis is clinical plus with urine tests. Withdrawal can be treated by substitution with a long-acting opioid (eg, methadone) or buprenorphine (a mixed opioid agonist-antagonist).

"Opioid" is a term for a number of natural substances (originally derived from the opium poppy) and their semisynthetic and synthetic analogues that bind to specific opioid receptors. Opioids, which are potent analgesics with a limited role in management of cough and diarrhea, are also common drugs of abuse because of their wide availability and euphoriant properties (see also p. 1623).

Pathophysiology

There are 3 main opioid receptors: delta, kappa, and mu. They occur throughout the CNS but particularly in areas and tracts associated with pain perception. Receptors are also located in some sensory nerves, on mast cells, and in some cells of the GI tract.

Opioid receptors are stimulated by endogenous endorphins, which generally produce analgesia and a sense of well-being. Opioids are used therapeutically primarily as analgesics. Opioids vary in their receptor activity, and some (eg, buprenorphine) have combined agonist and antagonist actions. Compounds with pure antagonist activity (eg, naloxone, naltrexone) are available.

Exogenous opioids can be taken by almost any route: orally, intravenously, subcutaneously, rectally,

through the nasal membranes, or inhaled as smoke. Peak effects are reached about 10 min after IV injection, 10 to 15 min after nasal insufflation, and 90 to 120 min after oral ingestion, although time to peak effects and duration of effect vary considerably depending on the specific drug.

Chronic effects: Tolerance develops quickly, with escalating dose requirements. Tolerance to the various effects of opioids frequently develops unevenly. Heroin users, for example, may become relatively tolerant to the drug's euphoric and respiratory depression effects but continue to have constricted pupils and constipation.

A minor withdrawal syndrome may occur after only several days' use. Severity of the syndrome increases with the size of the opioid dose and the duration of dependence.

Long-term effects of the opioids themselves are minimal; even decades of methadone use appear to be well tolerated physiologically, although some long-term opioid users experience chronic constipation, excessive sweating, peripheral edema, drowsiness, and decreased libido. However, many long-term users who inject opioids have adverse effects from contaminants (eg, talc) and adulterants (eg, nonprescription stimulant drugs) and cardiac, pulmonary, and hepatic damage due to infections such as HIV infection and hepatitis B or C, which are spread by needle sharing and nonsterile injection techniques (see p. 1509).

Pregnancy: Use of opioids during pregnancy can result in physical dependence in the fetus (see p. 2800).

Symptoms and Signs

Acute effects: Acute intoxication is characterized by euphoria and drowsiness. Mast cell effects (eg, flushing, itching) are common, particularly with morphine. GI effects include nausea, vomiting, decreased bowel sounds, and constipation.

Toxicity or overdose: The main toxic effect is decreased respiratory rate and depth, which can progress to apnea. Other complications (eg, pulmonary edema, which usually develops within minutes to a few hours after opioid overdose) and death result primarily from hypoxia. Pupils are miotic. Delirium, hypotension, bradycardia, decreased body temperature, and urinary retention may also occur.

Normeperidine, a metabolite of meperidine, accumulates with repeated use (including therapeutic); it stimulates the CNS and may cause seizure activity.

Serotonin syndrome (see p. 3269) occasionally occurs when fentanyl, meperidine, or oxycodone is taken concomitantly with other drugs that have serotonergic effects (eg, SSRIs, monoamine oxidase inhibitors). This syndrome consists of one or more of the following:

- Hypertonia
- Tremor and hyperreflexia
- Spontaneous clonus
- Inducible clonus plus agitation or diaphoresis
- Ocular clonus plus agitation or diaphoresis
- Temperature > 38° plus ocular or inducible clonus

Withdrawal: The withdrawal syndrome usually includes symptoms and signs of CNS hyperactivity. Onset and duration of the syndrome depend on the specific drug and its half-life. Symptoms may appear as early as 4 h after the last dose of heroin, peak within 48 to 72 h, and subside after about a week. Anxiety and a craving for the drug are followed by increased resting respiratory rate (> 16 breaths/min), usually with diaphoresis, yawning, lacrimation, rhinorrhea, mydriasis, and stomach cramps. Later, piloerection

(gooseflesh), tremors, muscle twitching, tachycardia, hypertension, fever and chills, anorexia, nausea, vomiting, and diarrhea may develop. Opioid withdrawal does not cause fever, seizures, or altered mental status. Although it may be distressingly symptomatic, opioid withdrawal is not fatal.

The withdrawal syndrome in people who were taking methadone (which has a long half-life) develops more slowly and may be less acutely severe than heroin withdrawal, although users may describe it as worse. Even after the withdrawal syndrome remits, lethargy, malaise, anxiety, and disturbed sleep may persist up to several months. Drug craving may persist for years.

Diagnosis

Diagnosis is usually made clinically and sometimes with urine drug testing (see p. 1510); laboratory tests are done as needed to identify drug-related complications. Drug levels are not measured.

Treatment

- Supportive therapy
- For withdrawal, sometimes drug therapy (eg, with an opioid agonist, opioid agonist-antagonist, opioid antagonist, or clonidine)

Toxicity or overdose: Treatment to maintain the airway and support breathing is the first priority.

- Naloxone 0.4 mg IV
- Sometimes endotracheal intubation

Patients with spontaneous respirations can be treated with an opioid antagonist, typically naloxone 0.4 mg IV (for children < 20 kg, 0.1 mg/kg); naloxone has no agonist activity and a very short half-life (see Table 340-8 on p. 3345). Naloxone rapidly reverses unconsciousness and apnea due to an opioid in most patients. If IV access is not immediately available, IM or sc administration is also effective. A 2nd or 3rd dose can be given if there is no response within 2 min. Almost all patients respond to three 0.4-mg doses. If they do not, the patient's condition is unlikely to be due to an opioid overdose, although massive opioid overdose may require higher doses of naloxone. Because some patients become agitated, delirious, and combative as consciousness returns and because naloxone precipitates acute withdrawal, soft physical restraints should be applied before naloxone is given. To ameliorate withdrawal in long-term users, some experts suggest titrating very small doses of naloxone (0.1 mg) when the clinical situation does not require emergency total reversal.

Apneic patients require endotracheal intubation. These patients should probably not receive total naloxone reversal because they may become agitated and belligerent when they suddenly regain consciousness.

In general, patients treated for overdose should be hospitalized and observed for at least 24 h because the duration of action of naloxone is less than that of some opioids, and overdose symptoms can redevelop. Respiratory depression may recur within several hours, especially with methadone or sustained-released oxycodone or morphine tablets. If respiratory depression recurs, naloxone should be readministered at an appropriate dose. Continuous naloxone infusion may be helpful for recurrent respiratory depression; two thirds of the dose that relieved respiratory depression is given hourly. Patients should be observed until no naloxone pharmacologic activity is present and they have no opioid-related symptoms. The serum half-life of naloxone is about 1 h, so an observation period of 2 to 3 h after use of naloxone should clarify disposition. The half-life of IV heroin is relatively short, and recurrent respiratory depression after naloxone reversal of IV heroin is rare.

Acute pulmonary edema is treated with supplemental O_2 and often noninvasive or invasive modalities of breathing support (eg, bilevel positive airway pressure [BiPAP], endotracheal intubation).

Withdrawal and detoxification: Treatment may involve several strategies:

• No treatment ("cold turkey")

• Substitution with methadone or buprenorphine

• Clonidine to relieve symptoms

• Long-term support and possibly naltrexone

The withdrawal syndrome is self-limited and, although severely uncomfortable, is not life threatening. Minor metabolic and physical withdrawal effects may persist up to 6 mo. Withdrawal is typically managed in outpatient settings, unless patients require hospitalization for concurrent medical or mental health problems.

Options for management of withdrawal include allowing the process to run its course ("cold turkey") after the patient's last opioid dose and giving another opioid (substitution) that can be tapered on a controlled schedule. Clonidine can provide some symptom relief during withdrawal.

Methadone substitution is the preferred method of managing opioid withdrawal for more seriously addicted patients because at appropriate doses, it has a long half-life and less profound sedation and euphoria. Any physician can initiate methadone substitution during hospitalization or for 3 days in an outpatient setting, but further treatment is continued in a licensed methadone treatment program. Methadone is given orally in the smallest amount that prevents severe but not necessarily all symptoms of withdrawal. Typical dose range is 15 to 30 mg once/day; doses ≥ 25 mg can result in dangerous levels of sedation in patients who have not developed tolerance. Symptom scales are available for estimating the appropriate dose. Higher doses should be given when evidence of withdrawal is observed. After the appropriate dose has been established, it should be reduced progressively by 10 to 20%/day unless the decision is made to continue the drug at a stable dose (methadone maintenance—see p. 1515). During tapering of the drug, patients commonly become anxious and request more of the drug. Methadone withdrawal for addicts who have been in a methadone maintenance program may be particularly difficult because their dose of methadone may be as high as 100 mg once/day; in these patients, the dose should be gradually reduced to 60 mg once/day over several weeks before attempting complete detoxification.

Buprenorphine, a mixed opioid agonist-antagonist usually given sublingually, also has been successfully used in withdrawal. It is available in a combination formulation with naloxone to prevent diversion to IV use. The first dose is given when the first signs of withdrawal appear. The dose needed to effectively control severe symptoms is titrated as quickly as possible; sublingual doses of 8 to 16 mg/day are typically used. Buprenorphine is then tapered over several weeks. Protocols for using buprenorphine for detoxification or maintenance therapy are available at the US Department of Health and Human Services web site.

Clonidine, a centrally acting adrenergic drug, can suppress symptoms and signs of opioid withdrawal. Starting dosages are 0.1 mg po q 4 to 6 h and may be increased to 0.2 mg po q 4 to 6 h as tolerated. Clonidine can cause hypotension and drowsiness, and its withdrawal may precipitate restlessness, insomnia, irritability, tachycardia, and headache.

Rapid and ultrarapid protocols have been evaluated for managing withdrawal and detoxification. In rapid protocols, combinations of naloxone, nalmefene, and naltrexone are used to induce withdrawal, and clonidine and various adjuvant drugs are used to suppress withdrawal symptoms. Some rapid protocols use buprenorphine to suppress opioid withdrawal symptoms. Ultrarapid protocols may use large boluses of naloxone and diuretics to enhance excretion of the opioids while patients are under general anesthesia; these ultrarapid protocols are not recommended because they have a high risk of complications and no substantial additional benefit.

Clinicians must understand that detoxification is not treatment per se. It is only the first step and must be followed by an ongoing treatment program, which may involve various kinds of counseling and possibly nonopioid antagonists (eg, naltrexone).

Opioid Abuse and Rehabilitation

Heroin is commonly abused, and abuse of prescription analgesic opioids (eg, morphine, oxycodone, hydrocodone, fentanyl) is increasing; some of the increase is due to people who began taking them for legitimate medical purposes. Patients with chronic pain requiring long-term use should not be routinely labeled addicts, although they commonly have tolerance and physical dependence.

Treatment

• For severe, relapsing dependence, maintenance preferred to opioid withdrawal

• For maintenance, buprenorphine or methadone

• Ongoing counseling and support

Physicians must be fully aware of federal, state, and local regulations concerning use of an opioid drug to treat an addict. To comply, physicians must establish the existence of physical opioid dependence. In the US, treatment is further complicated by negative societal attitudes toward addicts (including the attitudes of law enforcement officers, physicians, and other health care practitioners) and toward treatment programs, which some view as abetting drug consumption. In most cases, physicians should refer opioid-dependent patients to specialized treatment centers. If trained to do so, physicians may provide office-based treatment for selected patients. In European countries, access to methadone or buprenorphine maintenance programs and alternative maintenance strategies is easier, and the stigma attached to prescribing psychoactive drugs is less.

Maintenance: Long-term maintenance using an oral opioid such as methadone or buprenorphine (an opioid agonist-antagonist) is an alternative to opioid substitution with tapering. Oral opioids suppress withdrawal symptoms and drug craving without providing a significant high or oversedation and, by eliminating the supply problems of addicts, enable them to be socially productive. In the US, thousands of opioid addicts are in licensed methadone maintenance programs. For many, such programs work. However, because the participants continue to take an opioid, many people in society disapprove of these programs.

Eligibility criteria include the following:

• A positive drug screen for opioids

• Physical dependence for > 1 yr of continuous opioid use or intermittent use for even longer

• Evidence of withdrawal or physical findings confirming drug use

Clinicians and patients need to decide whether a withdrawal (detoxification) or opioid maintenance approach is indicated. Generally, patients with severe, chronic, relapsing dependence do much better with opioid maintenance. Withdrawal and detoxification, although effective in the short term, have poor outcomes in patients with severe opioid dependence. Whichever course is chosen, it must be accompanied by ongoing counseling and supportive measures.

Methadone is commonly used. Physicians can begin the substitution, but then use of methadone must be supervised in a licensed methadone treatment program.

Buprenorphine is being used increasingly for maintenance. Its effectiveness is comparable to that of methadone, and because it blocks receptors, it inhibits concomitant illicit use of heroin or other opioids. Buprenorphine can be prescribed for office-based treatment by specially trained physicians, including primary care physicians, who have received the required training and have been certified by the federal government. The typical dosage is an 8- or 16-mg sublingual tablet once/day. Many patients prefer this option because it eliminates the need for attending a methadone clinic. Buprenorphine is also available in combination with naloxone; the addition of naloxone may further discourage illicit opioid use. The combination formulation is used in office-based treatment.

Naltrexone, an opioid antagonist, blocks the effects of heroin. The usual dosage is 50 mg po once/day or 350 mg/wk po in 2 or 3 divided doses. A once-monthly depot IM formulation is also available. Because naltrexone is an opioid antagonist and has no direct agonist effects on opioid receptors, naltrexone is often unacceptable to opioid-dependent patients, especially those who have chronic, relapsing opioid dependence. For such patients, opioid maintenance treatment is much more effective. Naltrexone may be useful for patients with less severe dependence, early-stage opioid dependence, and strong motivation to remain abstinent. For example, opioid-dependent health care practitioners whose future employment is at risk if opioid use persists may be excellent candidates for naltrexone.

Levomethadyl acetate (LAAM), a longer-acting opioid related to methadone, is no longer used because it causes QT-interval abnormalities in some patients. LAAM could be used only 3 times/wk, thereby reducing the expense and problems of daily client visits or take-home drugs. A dose of 100 mg 3 times/wk is comparable to methadone 80 mg once/day.

Support: Most treatment of opioid dependence occurs in outpatient settings, typically in licensed opioid maintenance programs but increasingly in physician's offices.

The therapeutic community concept, pioneered by Daytop Village and Phoenix House, involves nondrug treatment in communal residential centers, where drug users receive training, education, and redirection to help them build new lives. Residency is usually 15 mo. These communities have helped, even transformed, some users. However, initial dropout rates are extremely high. Questions of how well these communities work, how many will be opened, and how much funding society will give remain unanswered.

Alcohol

Alcohol (ethanol) is a CNS depressant. Large amounts consumed rapidly can cause respiratory depression, coma, and death. Large amounts chronically consumed damage the liver and many other organs. Alcohol withdrawal manifests as a continuum, ranging from tremor to seizures, hallucinations, and life-threatening autonomic instability in severe withdrawal (delirium tremens). Diagnosis is clinical.

About 45 to 50% of adults are current drinkers, 20% are former drinkers, and 30 to 35% are lifetime abstainers. For most drinkers, the frequency and amount of alcohol consumption does not impair physical or mental health or the ability to safely carry out daily activities. However, acute alcohol intoxication is a significant factor in injuries, particularly those due to interpersonal violence, suicide, and motor vehicle crashes. Chronic abuse interferes with the ability to socialize and work. About 7 to 10% of adults meet criteria for an alcohol use disorder (abuse or dependence) in any given year. Binge drinking, defined as consuming ≥ 5 drinks per occasion for men and ≥ 4 drinks per occasion for women, is a particular problem among younger people.

Pathophysiology

One serving of alcohol (one 12-oz can of beer, one 6-oz glass of wine, or 1.5 oz of distilled liquor) contains 10 to 15 g of ethanol. Alcohol is absorbed into the blood mainly from the small bowel, although some is absorbed from the stomach. Alcohol accumulates in blood because absorption is more rapid than oxidation and elimination. The concentration peaks about 30 to 90 min after ingestion if the stomach was previously empty. About 5 to 10% of ingested alcohol is excreted unchanged in urine, sweat, and expired air; the remainder is metabolized mainly by the liver, where alcohol dehydrogenase converts ethanol to acetaldehyde. Acetaldehyde is ultimately oxidized to CO_2 and water at a rate of 5 to 10 mL/h (of absolute alcohol); each milliliter yields about 7 kcal. Alcohol dehydrogenase in the gastric mucosa accounts for some metabolism; much less gastric metabolism occurs in women.

Alcohol exerts its effects by several mechanisms. Alcohol binds directly to γ-aminobutyric acid (GABA) receptors in the CNS, causing sedation. Alcohol also directly affects cardiac, hepatic, and thyroid tissue.

Chronic effects: Tolerance to alcohol develops rapidly; similar amounts cause less intoxication.

Tolerance is caused by adaptational changes of CNS cells (cellular, or pharmacodynamic, tolerance) and by induction of metabolic enzymes. People who develop tolerance may reach an incredibly high blood alcohol content (BAC). However, ethanol tolerance is incomplete, and considerable intoxication and impairment occur with a large enough amount. But even these drinkers may die of respiratory depression secondary to alcohol overdose. Alcohol-tolerant people are susceptible to alcoholic ketoacidosis (see p. 886), especially during binge drinking. Alcohol-tolerant people are cross-tolerant of many other CNS depressants (eg, barbiturates, nonbarbiturate sedatives, benzodiazepines).

The physical dependence accompanying tolerance is profound, and withdrawal has potentially fatal adverse effects.

Chronic heavy alcohol intake typically leads to liver disorders (eg, fatty liver, alcoholic hepatitis, cirrhosis); the amount and duration required vary (see p. 235). Patients with a severe liver disorder often have coagulopathy due to decreased hepatic synthesis of coagulation factors, increasing the risk of significant bleeding due to trauma (eg, from falls or vehicle crashes) and of GI bleeding (eg, due to gastritis, from esophageal varices due to portal hypertension); alcohol abusers are at particular risk of GI bleeding.

Chronic heavy intake also commonly causes the following:

- Gastritis
- Pancreatitis
- Cardiomyopathy, often accompanied by arrhythmias and hypertension
- Peripheral neuropathy
- Brain damage, including Wernicke's encephalopathy, Korsakoff's psychosis, Marchiafava-Bignami disease, and alcoholic dementia
- Certain cancers (eg, head and neck, esophageal), especially when drinking is combined with smoking

Indirect long-term effects include undernutrition, particularly vitamin deficiencies.

On the other hand, low to moderate levels of alcohol consumption (≤ 1 to 2 drinks/day) may decrease the risk of death due to cardiovascular disorders. Numerous explanations, including increased high density lipoprotein (HDL) levels and a direct antithrombotic effect, have been suggested. Nonetheless, alcohol should not be recommended for this purpose, especially when there are several safer, more effective approaches to reduce cardiovascular risk.

Special populations: Young children who drink alcohol are at significant risk of hypoglycemia because alcohol impairs gluconeogenesis and their smaller stores of glycogen are rapidly depleted. Women may be more sensitive than men, even on a per-weight basis, because their gastric (first-pass) metabolism of alcohol is less. Drinking during pregnancy increases the risk of fetal alcohol syndrome (see p. 2799).

Symptoms and Signs

Acute effects: Symptoms progress proportionately to the BAC. Actual levels required to cause given symptoms vary with tolerance, but in typical users

- 20 to 50 mg/dL: Tranquility, mild sedation, and some decrease in fine motor coordination
- 50 to 100 mg/dL: Impaired judgment and a further decrease in coordination
- 100 to 150 mg/dL: Unsteady gait, nystagmus, slurred speech, loss of behavioral inhibitions, and memory impairment
- 150 to 300 mg/dL: Delirium and lethargy (likely)

Emesis is common with moderate to severe intoxication; because emesis usually occurs with obtundation, aspiration is a significant risk.

In most US states, the legal definition of intoxication is a BAC of ≥ 0.08 to 0.10% (≥ 80 to 100 mg/dL); 0.08 is used most commonly.

Toxicity or overdose: In alcohol-naive people, a BAC of 300 to 400 mg/dL often causes unconsciousness, and a BAC ≥ 400 mg/dL may be fatal. Sudden death due to respiratory depression or arrhythmias may occur, especially when large quantities are drunk rapidly. This problem is emerging in US colleges but has been known in other countries where it is more common. Other common effects include hypotension and hypoglycemia.

The effect of a particular BAC varies widely; some chronic drinkers seem unaffected and appear to function normally with a BAC in the 300 to 400 mg/dL range, whereas non-drinkers and social drinkers are impaired at a BAC that is inconsequential in chronic drinkers.

Chronic effects: Stigmata of chronic use include Dupuytren's contracture of the palmar fascia, vascular spiders, and, in men, signs of hypogonadism and feminization (eg, smooth skin, lack of male-pattern baldness, gynecomastia, testicular atrophy). Undernutrition may lead to enlarged parotid glands.

Withdrawal: A continuum of symptoms and signs of CNS (including autonomic) hyperactivity may accompany cessation of alcohol intake.

A mild withdrawal syndrome includes tremor, weakness, headache, sweating, hyperreflexia, and GI symptoms. Symptoms usually begin within about 6 h of cessation. Some patients have generalized tonic-clonic seizures (called alcoholic epilepsy, or rum fits) but usually not > 2 in short succession.

Alcoholic hallucinosis (hallucinations without other impairment of consciousness) follows abrupt cessation from prolonged, excessive alcohol use, usually within 12 to 24 h. Hallucinations are typically visual. Symptoms may also include auditory illusions and hallucinations that frequently are accusatory and threatening; patients are usually apprehensive and may be terrified by the hallucinations and by vivid, frightening dreams. The syndrome may resemble schizophrenia, although thought is usually not disordered and the history is not typical of schizophrenia. Symptoms do not resemble the delirious state of an acute organic brain syndrome as much as does delirium tremens (DT) or other pathologic reactions associated with withdrawal. Consciousness remains clear, and the signs of autonomic lability that occur in DT are usually absent. When hallucinosis occurs, it usually precedes DT and is transient.

DT usually begins 48 to 72 h after alcohol withdrawal; anxiety attacks, increasing confusion, poor sleep (with frightening dreams or nocturnal illusions), profuse sweating, and severe depression also occur. Fleeting hallucinations that arouse restlessness, fear, and even terror are common. Typical of the initial delirious, confused, and disoriented state is a return to a habitual activity; eg, patients frequently imagine that they are back at work and attempt to do some related activity. Autonomic lability, evidenced by diaphoresis and increased pulse rate and temperature, accompanies the delirium and progresses with it. Mild delirium is usually accompanied by marked diaphoresis, a pulse rate of 100 to 120 beats/min, and a temperature of 37.2 to 37.8° C. Marked delirium, with gross disorientation and cognitive disruption, is accompanied by significant restlessness, a pulse of > 120 beats/min, and a temperature of > 37.8° C; risk of death is high.

During DT, patients are suggestible to many sensory stimuli, particularly to objects seen in dim light. Vestibular disturbances may cause them to believe that the floor is moving, the walls are falling, or the room is rotating. As the delirium progresses, resting tremor of the hand develops, sometimes extending to the head and trunk. Ataxia is marked; care must be taken to prevent self-injury. Symptoms vary among patients but are usually the same for a particular patient with each recurrence.

Diagnosis

• Usually clinical

• Acute: BAC, evaluation to rule out hypoglycemia and occult trauma

• Chronic: CBC, Mg, liver function tests, and PT/PTT

• Withdrawal: Evaluation to rule out CNS injury and infection

In acute intoxication, laboratory tests, except for fingerstick glucose to rule out hypoglycemia and tests to determine BAC, are generally not helpful; diagnosis is usually made clinically. Confirmation by breath or blood alcohol levels is useful for legal purposes (eg, to document intoxication in drivers or employees who appear impaired). However, finding a low BAC in patients who have altered mental status and smell of alcohol is helpful because it expedites the search for an alternate cause. Clinicians should not assume that a high BAC in patients with apparently minor trauma accounts for their obtundation, which may be due to intracranial injury or other abnormalities. Such patients should also have toxicology tests to search for evidence of toxicity due to other substances.

Chronic alcohol abuse and dependence are clinical diagnoses; experimental markers of long-term use have not proved sufficiently sensitive or specific for general use. However, heavy alcohol users may have a number of metabolic derangements that are worth screening for, so CBC, electrolytes (including Mg), liver function tests including coagulation profile (PT/PTT), and serum albumin are often recommended.

In severe withdrawal and toxicity, symptoms may resemble those of CNS injury or infection, so medical evaluation with CT and lumbar puncture may be needed. Patients with mild symptoms do not require routine testing unless improvement is not marked within 2 to 3 days.

Treatment

• Supportive measures

• For withdrawal, benzodiazepines

Toxicity or overdose: Treatment may include the following:

• Airway protection

• Sometimes IV fluids with thiamin, Mg, and vitamins

The first priority is ensuring an adequate airway; endotracheal intubation and mechanical ventilation are required for apnea or inadequate respirations. IV hydration is needed for hypotension or evidence of volume depletion but does not significantly enhance ethanol clearance. When IV fluids are used, a single dose of thiamin 100 mg IV is given to treat or prevent Wernicke's encephalopathy. Many clinicians also add multivitamins and Mg to the IV fluids.

Disposition of the acutely intoxicated patient depends on clinical response, not a specific BAC.

Withdrawal: Patients with severe withdrawal or DT should be managed in an ICU until these symptoms abate. Treatment may include the following to prevent Wernicke-Korsakoff syndrome and other complications:

• IV thiamin

• Benzodiazepines

Thiamin 100 mg IV is given to prevent Wernicke-Korsakoff syndrome.

Alcohol-tolerant people are cross-tolerant of some drugs commonly used to treat withdrawal (eg, benzodiazepines).

Benzodiazepines are the mainstay of therapy. Dosage and route depend on degree of agitation, vital signs, and mental status. Diazepam, given 5 to 10 mg IV or po hourly until sedation occurs, is a common initial intervention; lorazepam 1 to 2 mg IV or po is an alternative. Chlordiazepoxide 50 to 100 mg po q 4 to 6 h, then tapered, is an older acceptable alternative for less severe cases of withdrawal. Phenobarbital may help if benzodiazepines are ineffective, but respiratory depression is a risk with concomitant use. Phenothiazines and haloperidol are not recommended initially because they may lower the seizure threshold. For patients with a significant liver disorder, a short-acting benzodiazepine (lorazepam) or one metabolized by glucuronidation (oxazepam) is preferred. (NOTE: Benzodiazepines may cause intoxication, physical dependence, and withdrawal in alcoholics and therefore should not be continued after the detoxification period. Carbamazepine 200 mg po qid may be used as an alternative and then tapered.) For severe hyperadrenergic activity or to reduce benzodiazepine requirements, short-term therapy (12 to 48 h) with titrated β-blockers (eg, metoprolol 25 to 50 mg po or 5 mg IV q 4 to 6 h) and clonidine 0.1 to 0.2 mg IV q 2 to 4 h can be used.

A **seizure,** if brief and isolated, needs no specific therapy; however, some clinicians routinely give a single dose of lorazepam 1 to 2 mg IV as prophylaxis against another seizure. Repeated or longer-lasting (ie, > 2 to 3 min) seizures should be treated and often respond to lorazepam 1 to 3 mg IV. Routine use of phenytoin is unnecessary and unlikely to be effective. Outpatient therapy with phenytoin is rarely indicated for patients with simple alcohol withdrawal seizures when no other source of seizure activity has been identified because seizures occur only under the stress of alcohol withdrawal, and patients who are withdrawing or heavily drinking may not take the anticonvulsant.

DT may be fatal and thus must be treated promptly with high-dose IV benzodiazepines, preferably in an ICU. Dosing is higher and more frequent than in mild withdrawal. Very high doses of benzodiazepines may be required, and there is no maximum dose or specific treatment regimen. Diazepam 5 to 10 mg IV or lorazepam 1 to 2 mg IV q 10 min is given as needed to control delirium; some patients require several hundred milligrams over the first few hours. Patients refractory to high-dose benzodiazepines may respond to phenobarbital 120 to 240 mg IV q 20 min as needed. Severe drug-resistant DT can be treated with a continuous infusion of lorazepam, diazepam, midazolam, or propofol, usually with concomitant mechanical ventilation. Physical restraints should be avoided if possible to minimize additional agitation, but patients must not be allowed to elope, remove IVs, or otherwise endanger themselves. Intravascular volume must be maintained with IV fluids, and large doses of vitamins B and C, particularly thiamin, must be given promptly. Appreciably elevated temperature with DT is a poor prognostic sign.

Alcohol Problems and Rehabilitation

Definitions

At-risk drinking is defined solely by quantity and frequency of drinking:

- > 14 drinks/wk or 4 drinks per occasion for men
- > 7 drinks/wk or 3 drinks per occasion for women

Compared with lesser amounts, these amounts are associated with increased risk of a wide variety of medical and psychosocial complications.

Alcohol abuse refers to a maladaptive pattern of episodic drinking that results in failure to fulfill obligations, drinking in physically hazardous situations (eg, driving, boating), legal problems, or social and interpersonal problems without evidence of dependence.

Alcohol dependence refers to frequent consumption of large amounts of alcohol with ≥ 3 of the following:

- Tolerance
- Withdrawal symptoms

• Drinking larger amounts than intended

• Persistent desire to reduce use without success

• Substantial time spent obtaining, drinking, or recovering from alcohol

• Sacrifice of other life events for drinking

• Continued use despite physical or psychologic problems

Alcoholism is often used as an equivalent term for alcohol dependence, especially when drinking results in significant toxicity and tissue damage.

Etiology

The maladaptive pattern of drinking that constitutes alcohol abuse may begin with a desire to reach a state of feeling high. Some drinkers who find the feeling rewarding then focus on repeatedly reaching that state. Many who abuse alcohol chronically have certain personality traits: feelings of isolation, loneliness, shyness, depression, dependency, hostile and self-destructive impulsivity, and sexual immaturity. Alcoholics may come from a broken home and have a disturbed relationship with their family. Societal factors—attitudes transmitted through the culture or child rearing—affect patterns of drinking and consequent behavior. However, such generalizations should not obscure the fact that alcohol use disorders can occur in anyone, regardless of their age, sex, background, ethnicity, or social situation. Thus, clinicians should screen for alcohol problems in all patients.

The incidence of alcohol abuse and dependence is higher in biologic children of people with alcohol problems than in adoptive children, and the percentage of biologic children of alcoholics who are problem drinkers is greater than that of the general population. There is evidence of genetic or biochemical predisposition, including data that suggest some people who become alcoholics are less easily intoxicated; ie, they have a higher threshold for CNS effects.

Symptoms and Signs

Serious social consequences usually occur. Frequent intoxication is obvious and destructive; it interferes with the ability to socialize and work. Injuries are common. Eventually, failed relationships and job loss due to absenteeism may result. People may be arrested because of alcohol-related behavior or be apprehended for driving while intoxicated, often losing driving privileges for repeated offenses; in most US states, the maximum legal blood alcohol concentration (BAC) while driving is 80 mg/dL (0.08%), and this level is likely to be reduced in the future.

Diagnosis

• Clinical evaluation

• Screening

Some alcohol-related problems are diagnosed when people seek medical treatment for their drinking or for obvious alcohol-related illness (eg, delirium tremens, cirrhosis). However, many of these people remain unrecognized for a long time. Female alcoholics are, in general, more likely to drink alone and are less likely to manifest some of the social signs. Therefore, many governmental and professional organizations recommend alcohol screening during routine health care visits. A scaled approach (see Table 160-2) can help

[**Table 160-2.** Levels of Screening for Alcohol Problems]

identify patients who require more detailed questioning; several validated detailed questionnaires are available.

Treatment

• Rehabilitation programs

• Outpatient counseling

• Self-help groups

• Consideration of drugs (eg, naltrexone, disulfiram)

All patients should be counseled to decrease their alcohol use to below at-risk levels.

For patients identified as at-risk drinkers, treatment may begin with a brief discussion of the medical and social consequences and a recommendation to reduce or cease drinking, with follow-up regarding compliance (see
Table 160-3).

For patients with more serious problems, particularly after less intensive measures have been unsuccessful, a rehabilitation program is often the best approach. Rehabilitation programs combine psychotherapy, including one-on-one and group therapy, with medical supervision. For most patients, outpatient rehabilitation is sufficient; how long patients remain enrolled in programs varies, typically weeks to months, but longer if needed. Inpatient rehabilitation programs are reserved for patients with more severe alcohol dependence and those with significant and comorbid medical, psychoactive, and substance abuse problems. Treatment duration is usually briefer (typically days to weeks) than that of outpatient programs and may be dictated in part by patients' insurance.

Psychotherapy involves techniques that enhance motivation and teach patients to avoid circumstances that precipitate drinking. Social support of abstinence, including the support of family and friends, is important.

Maintenance: Maintaining sobriety is difficult. Patients should be warned that after a few weeks, when they have recovered from their last bout, they are likely to find an excuse to drink. They should also be told that although they may be able to practice controlled drinking for a few days or, rarely, a few weeks, they will most likely lose control eventually.

In addition to the counseling provided in outpatient and inpatient alcohol treatment programs, self-help groups and certain drugs may help prevent relapse in some patients.

Alcoholics Anonymous (AA) is the most common self-help group. Patients must find an AA group they feel comfortable in. AA provides patients with nondrinking friends who are always available and a nondrinking environment in which to socialize. Patients also hear others discuss every rationalization they have ever used for their own drinking. The help they give other alcoholics may give them the self-regard and confidence formerly found only in alcohol. Many alcoholics are reluctant to go to AA and find individual counseling or group or family treatment more acceptable. Alternative organizations, such as LifeRing Recovery (Secular Organizations for Sobriety), exist for patients seeking another approach.

Drug therapy should be used with counseling rather than as sole treatment.

Disulfiram, the first drug available to prevent relapse in alcohol dependence, interferes with the metabolism of acetaldehyde (an intermediary product in the oxidation of alcohol) so that acetaldehyde accumulates. Drinking alcohol within 12 h of taking disulfiram causes

[**Table 160-3.** Brief Interventions for Alcohol Problems]

facial flushing in 5 to 15 min, then intense vasodilation of the face and neck with suffusion of the conjunctivae, throbbing headache, tachycardia, hyperpnea, and sweating. With high doses of alcohol, nausea and vomiting may follow in 30 to 60 min and may lead to hypotension, dizziness, and sometimes fainting and collapse. The reaction can last up to 3 h. Few patients risk drinking alcohol while taking

disulfiram because of the intense discomfort. Drugs that contain alcohol (eg, tinctures; elixirs; some OTC liquid cough and cold preparations, which contain as much as 40% alcohol) must also be avoided. Disulfiram is contraindicated during pregnancy and in patients with cardiac decompensation. It may be given on an outpatient basis after 4 or 5 days of abstinence. The initial dosage is 0.5 g po once/day for 1 to 3 wk, followed by a maintenance dosage of 0.25 g once/day. Effects may persist for 3 to 7 days after the last dose. Periodic physician visits are needed to encourage continuation of disulfiram as part of an abstinence program. Disulfiram's general usefulness has not been established, and many patients are nonadherent. Adherence usually requires adequate social support, such as observation of drinking. For these reasons, use of disulfiram is now limited. Disulfiram is most effective when given under close supervision to highly motivated patients.

Naltrexone, an opioid antagonist (see p. 1515), decreases the relapse rate and number of drinking days in most patients who take it consistently. Naltrexone 50 mg po once/day is typically given, although there is evidence that higher doses (eg, 100 mg once/day) may be more effective in some patients. Even with counseling, adherence rates with oral naltrexone are modest. A long-acting depot form is also available: 380 mg IM once/mo. Naltrexone is contraindicated in patients with acute hepatitis or liver failure and in those who are opioid dependent.

Acamprosate, a synthetic analogue of γ-aminobutyric acid, is given as 2 g po once/day. Acamprosate may decrease the relapse rate and number of drinking days in patients who relapse.

Nalmefene, an opioid antagonist, and topiramate are under study for their ability to decrease alcohol craving.

Wernicke's Encephalopathy

Wernicke's encephalopathy is characterized by acute onset of confusion, nystagmus, partial ophthalmoplegia, and ataxia due to thiamin deficiency. Diagnosis is primarily clinical. The disorder may remit with treatment, persist, or degenerate into Korsakoff's psychosis. Treatment consists of thiamin and supportive measures.

Wernicke's encephalopathy results from inadequate intake or absorption of thiamin plus continued carbohydrate ingestion. Severe alcoholism is a common underlying condition. Excessive alcohol intake interferes with thiamin absorption from the GI tract and hepatic storage of thiamin; the poor nutrition associated with alcoholism often precludes adequate thiamin intake. Wernicke's encephalopathy may also result from other conditions that cause prolonged undernutrition or vitamin deficiency (eg, recurrent dialysis, hyperemesis, starvation, gastric plication, cancer, AIDS). Loading carbohydrates in patients with thiamin deficiency (ie, refeeding after starvation or giving IV dextrose-containing solutions to high-risk patients) can trigger Wernicke's encephalopathy.

Not all thiamin-deficient alcohol abusers develop Wernicke's encephalopathy, suggesting that other factors may be involved. Genetic abnormalities that result in a defective form of transketolase, an enzyme that processes thiamin, may be involved.

Characteristically, CNS lesions are symmetrically distributed around the 3rd ventricle, aqueduct, and 4th ventricle. Changes in the mamillary bodies, dorsomedial thalamus, locus ceruleus, periaqueductal gray matter, ocular motor nuclei, and vestibular nuclei are common.

Symptoms and Signs

Clinical changes occur suddenly. Oculomotor abnormalities, including horizontal and vertical nystagmus and partial ophthalmoplegias (eg, lateral rectus palsy, conjugate gaze palsies), are common. Pupils may be abnormal; they are usually sluggish or unequal.

Vestibular dysfunction without hearing loss is common, and the oculovestibular reflex may be impaired. Gait ataxia may result from vestibular disturbances and cerebellar dysfunction; gait is wide-based and slow, with short-spaced steps.

Global confusion is often present; it is characterized by profound disorientation, indifference, inattention, drowsiness, or stupor. Peripheral nerve pain thresholds are often elevated, and many patients develop severe autonomic dysfunction characterized by sympathetic hyperactivity (eg, tremor, agitation) or hypoactivity (eg, hypothermia, postural hypotension, syncope). In untreated patients, stupor may progress to coma, then to death.

Diagnosis

• Clinical evaluation

Diagnosis is clinical and depends on recognition of underlying undernutrition or vitamin deficiency. There are no characteristic abnormalities in CSF, evoked potentials, brain imaging, or EEG. However, these tests, as well as laboratory tests (eg, blood tests, glucose, CBC, liver function tests, ABG measurements, toxicology screening), should be done to rule out other etiologies. Thiamin levels are not routinely measured.

Prognosis

Prognosis depends on timely diagnosis. If begun in time, treatment may correct all abnormalities. Ocular symptoms usually begin to abate within 24 h after early thiamin administration. Ataxia and confusion may persist days to months. Untreated, the disorder progresses; mortality is 10 to 20%. Of surviving patients, 80% develop Korsakoff psychosis; the combination is called Wernicke-Korsakoff syndrome.

Treatment

• Parenteral thiamin

• Parenteral Mg

Treatment consists of immediate administration of thiamin 100 mg IV or IM, continued daily for at least 3 to 5 days. Mg is a necessary cofactor in thiamin-dependent metabolism, and hypomagnesemia should be corrected using Mg sulfate 1 to 2 g IM or IV q 6 to 8 h or Mg oxide 400 to 800 mg po once/day. Supportive treatment includes rehydration, correction of electrolyte abnormalities, and general nutritional therapy, including multivitamins. Patients with advanced disease require hospitalization. Alcohol cessation is mandatory.

Because Wernicke's encephalopathy is preventable, all undernourished patients should be treated with parenteral thiamin (typically 100 mg IM followed by 50 mg po once/day) plus vitamin B_{12} and folate (1 mg po once/day for both), particularly if IV dextrose is necessary. Thiamin is also prudent before any treatment is begun in patients who present with a reduced level of consciousness. Patients who are undernourished should continue to receive thiamin as outpatients.

Korsakoff's Psychosis

Korsakoff's psychosis is a late complication of persistent Wernicke's encephalopathy and results in memory deficits, confusion, and behavioral changes.

Korsakoff's psychosis (Korsakoff's amnestic syndrome) occurs in 80% of untreated patients with Wernicke's encephalopathy. Why Korsakoff's psychosis develops in only some patients with Wernicke's encephalopathy is unclear. A severe or repeated attack of post-alcoholic delirium tremens can trigger Korsakoff's psychosis whether or not a typical attack of Wernicke's encephalopathy has occurred first.

Other triggers include head injury, subarachnoid hemorrhage, thalamic hemorrhage, thalamic ischemic stroke, and, infrequently, tumors affecting the paramedian posterior thalamic region.

Symptoms and Signs

Immediate memory is severely affected; retrograde and anterograde amnesia occurs in varying degrees.

Patients tend to draw on memory of remote events, which appears to be less affected than memory of recent events. Disorientation to time is common. Emotional changes are common; they include apathy, blandness, or mild euphoria with little or no response to events, even frightening ones. Spontaneity and initiative may be decreased.

Confabulation is often a striking early feature. Bewildered patients unconsciously fabricate imaginary or confused accounts of events they cannot recall; these fabrications may be so convincing that the underlying disorder is not detected.

Diagnosis

Diagnosis is based on typical symptoms in patients with a history of severe chronic alcohol dependence. Other causes of symptoms (eg, CNS injury or infection) must be ruled out.

Prognosis

Prognosis is fairly good for patients with head injury, subarachnoid hemorrhage, or both; the amnesia is transient. Prognosis is poor when the cause is thiamin deficiency or stroke; prolonged institutional care is required for about 25% of patients, and only about 20% recover completely. However, they may improve up to 12 to 24 mo after onset, and patients should not be prematurely institutionalized.

Treatment

Treatment consists of thiamin and adequate hydration.

Marchiafava-Bignami Disease

Marchiafava-Bignami disease is a rare demyelination of the corpus callosum that occurs in chronic alcoholics, predominantly men.

Pathology and circumstances link this disorder to osmotic demyelination syndrome (previously called central pontine myelinolysis), of which it may be a variant (see p. 828). In Marchiafava-Bignami disease, agitation and confusion occur with progressive dementia and frontal release signs. Some patients recover over several months; others experience seizures and coma, which may precede death.

Anxiolytics and Sedatives

Anxiolytics and sedatives (hypnotics) include benzodiazepines, barbiturates, and related drugs. High doses can cause stupor and respiratory depression, which is managed with intubation and mechanical ventilation. Chronic users may have a withdrawal syndrome of agitation and seizures, so dependence is managed by slow tapering with or without substitution (ie, with pentobarbital or phenobarbital).

The therapeutic benefit of anxiolytics and sedatives is well-established, but their value in alleviating stress and anxiety is also probably the reason that they are abused so frequently. Abused anxiolytics and sedatives include benzodiazepines, barbiturates, and other drugs taken to promote sleep.

Pathophysiology

Benzodiazepines and barbiturates potentiate γ-aminobutyric acid (GABA) at specific receptors thought to be located near GABA receptors. The exact mechanism of this potentiation process remains unclear but may be related to opening of chloride channels, producing a hyperpolarized state within the postsynaptic neuron.

Chronic effects: Patients taking high doses of sedatives frequently have difficulty thinking, slow speech and comprehension (with some dysarthria), poor memory, faulty judgment, narrowed attention span, and emotional lability. In susceptible patients, psychologic dependence on the drug may develop rapidly. The extent of physical dependence is related to dose and duration of use; eg, pentobarbital 200 mg/day taken

for many months may not induce significant tolerance, but 300 mg/day for > 3 mo or 500 to 600 mg/day for 1 mo may induce a withdrawal syndrome when the drug is stopped. Tolerance and tachyphylaxis develop irregularly and incompletely; thus, considerable behavioral, mood, and cognitive disturbances persist, even in regular users, depending on the dosage and the drug's pharmacodynamic effects. Some cross-tolerance exists between alcohol and barbiturates and nonbarbiturate anxiolytics and sedatives, including benzodiazepines. (Barbiturates and alcohol are strikingly similar in the dependence, withdrawal symptoms, and chronic intoxication they cause.)

Pregnancy: Prolonged use of barbiturates during pregnancy can cause withdrawal in the neonate (see p. 2799).

Symptoms and Signs

Toxicity or overdose: The signs of progressive anxiolytic and sedative intoxication are depression of superficial reflexes, fine lateral-gaze nystagmus, slightly decreased alertness with coarse or rapid nystagmus, ataxia, slurred speech, and postural unsteadiness.

Increasing toxicity can cause nystagmus on forward gaze, miosis, somnolence, marked ataxia with falling, confusion, stupor, respiratory depression, and, ultimately, death. Overdose of a benzodiazepine rarely causes hypotension, and these drugs do not cause arrhythmias.

Withdrawal: When intake of therapeutic doses of anxiolytics and sedatives is stopped or reduced below a critical level, a self-limited mild withdrawal syndrome can ensue. After only a few weeks, attempts to stop using the drug can exacerbate insomnia and result in restlessness, disturbing dreams, frequent awakening, and feelings of tension in the early morning.

Withdrawal from benzodiazepines is rarely life threatening. Symptoms can include tachypnea, tachycardia, tremulousness, hyperreflexia, confusion, and seizures. Onset may be slow because the drugs remain in the body a long time. Withdrawal may be most severe in patients who used drugs with rapid absorption and a quick decline in serum levels (eg, alprazolam, lorazepam, triazolam). Many people who misuse benzodiazepines have been or are heavy users of alcohol, and a delayed benzodiazepine withdrawal syndrome may complicate alcohol withdrawal.

Withdrawal from barbiturates taken in large doses causes an abrupt, potentially life-threatening withdrawal syndrome similar to delirium tremens. Occasionally, even after properly managed withdrawal over 1 to 2 wk, a seizure occurs. Without treatment, withdrawal of a short-acting barbiturate causes the following:

- Within the first 12 to 20 h: Increasing restlessness, tremulousness, and weakness
- By the 2nd day: More prominent tremulousness, sometimes increased deep tendon reflexes, and increased weakness
- During the 2nd and 3rd days: Seizures (in 75% of patients who were taking ≥ 800 mg/day), sometimes progressing to status epilepticus and death
- From the 2nd to the 5th day: Delirium, insomnia, confusion, frightening visual and auditory hallucinations, and often hyperpyrexia and dehydration

Diagnosis

- Clinical evaluation

Diagnosis is usually made clinically. Drug levels are not measured. Benzodiazepines and barbiturates are usually included in routine immunoassay-based urine drug screens (see p. 1510).

Treatment

• Airway protection

• Flumazenil considered

• Urine alkalinization for barbiturates

Toxicity or overdose: Acute intoxication generally requires nothing more than observation, although the airway and respirations should be carefully assessed. If ingestion was within 1 h, the gag reflex is preserved, and the patient can protect the airway, 50 g of activated charcoal may be given to reduce further absorption; however, this intervention has not been shown to reduce morbidity or mortality. Occasionally, intubation and mechanical ventilation are required.

The benzodiazepine receptor antagonist flumazenil can reverse severe sedation secondary to benzodiazepine overdose. Dose is 0.2 mg IV given over 30 sec; 0.3 mg may be given after 30 sec, followed by 0.5 mg q 1 min to total 3 mg. However, its clinical usefulness is not well-defined because most people who overdose on benzodiazepines recover with only supportive care, and occasionally flumazenil precipitates seizures. Contraindications to flumazenil include long-term benzodiazepine use (because flumazenil may precipitate withdrawal), an underlying seizure disorder, presence of twitching or other motor abnormalities, a concomitant epileptogenic drug overdose (especially of tricyclic antidepressants), and cardiac arrhythmias.

If barbiturate overdose is diagnosed, urine should be alkalinized to increase excretion.

Withdrawal and detoxification: Severe acute withdrawal requires hospitalization, preferably in an ICU, and use of appropriate doses of IV benzodiazepines.

One approach for managing sedative dependence is to withdraw the drug on a strict schedule while monitoring signs of withdrawal. Often, switching to a long-acting drug, which is easier to taper, is better.

As for alcohol withdrawal, patients going through anxiolytic or sedative withdrawal require close monitoring, preferably in an inpatient setting if a moderate to severe withdrawal reaction is expected.

Marijuana (Cannabis)

Marijuana is a euphoriant that can cause sedation or dysphoria in some users. Overdose does not occur. Psychologic dependence can develop with chronic use, but very little physical dependence is clinically apparent. Withdrawal is uncomfortable but requires only supportive treatment.

Marijuana is the most commonly used illicit drug; it is typically used episodically without evidence of social or psychologic dysfunction.

In the US, marijuana is commonly smoked in cigarettes, made from the flowering tops and leaves of the dried plant, or as hashish, the pressed resin of the plant. Much less commonly, marijuana is taken orally. Dronabinol, a synthetic oral form of the active ingredient, Δ-9-tetrahydrocannabinol (THC), is used to treat nausea and vomiting associated with cancer chemotherapy and to enhance appetite in AIDS patients.

Pathophysiology

Δ-9-THC binds at cannabinoid receptors, which are present throughout the brain.

Chronic effects: Any drug that causes euphoria and diminishes anxiety can cause dependence, and marijuana is no exception. However, heavy use and reports of inability to stop are unusual. Critics of marijuana cite much scientific data regarding adverse effects, but most claims of significant biologic effect are unsubstantiated. Findings are sparse even among relatively heavy users and in areas intensively investigated (eg, immunologic and reproductive function). However, high-dose smokers develop pulmonary symptoms (episodes of acute bronchitis, wheezing, coughing, and increased phlegm), and

pulmonary function may be altered, manifested as large airway changes of unknown significance. Even daily smokers do not develop obstructive airway disease. There is no evidence of increased risk of head and neck or airway cancers, as there is with tobacco. In a few case-control studies, diminished cognitive function was identified in small samples of long-term high-dose users; this finding needs to be confirmed. A sense of diminished ambition and energy is often described.

The effect of prenatal marijuana use on neonates is not clear. Decreased fetal weight has been reported, but when all factors (eg, maternal alcohol and tobacco use) are accounted for, the effect on fetal weight appears less. THC is secreted in breast milk. Although harm to breastfed infants has not been shown, breastfeeding mothers, like pregnant women, should avoid using marijuana.

Symptoms and Signs

Intoxication and withdrawal are not life threatening.

Acute effects: Within minutes, smoking marijuana produces a dreamy state of consciousness in which ideas seem disconnected, unanticipated, and free-flowing. Time, color, and spatial perceptions may be altered. In general, intoxication consists of a feeling of euphoria and relaxation (a high). These effects last 4 to 6 h after inhalation.

Many of the other reported psychologic effects seem to be related to the setting in which the drug is taken. Anxiety, panic reactions, and paranoia have occurred, particularly in naive users. Marijuana may exacerbate or even precipitate psychotic symptoms in schizophrenics, even those being treated with antipsychotics.

Physical effects are mild in most patients. Tachycardia, conjunctival injection, and dry mouth occur regularly. Concentration, sense of time, fine coordination, depth perception, tracking, and reaction time can be impaired for up to 24 h—all hazardous in certain situations (eg, driving, operating heavy equipment). Appetite often increases.

Withdrawal: Cessation after 2 to 3 wk of frequent, heavy use can cause a mild withdrawal syndrome, which typically begins about 12 h after the last use. Symptoms consist of insomnia, irritability, depression, nausea, and anorexia; symptoms peak at 2 to 3 days and last up to 7 days.

Diagnosis

• Clinical evaluation

Diagnosis is usually made clinically. Drug levels are not measured. Most routine urine drug screens include marijuana (see p. 1510).

Treatment

• Supportive measures

Treatment is usually unnecessary; for patients experiencing significant discomfort, treatment is supportive. Management of abuse typically consists of behavioral therapy in an outpatient drug treatment program.

Cocaine

Cocaine is a sympathomimetic drug with CNS stimulant and euphoriant properties. High doses can cause panic, schizophrenic-like symptoms, seizures, hyperthermia, hypertension, arrhythmias, stroke, aortic dissection, intestinal ischemia, and MI. Toxicity is managed with supportive care, including IV benzodiazepines (for agitation, hypertension, and seizures) and cooling techniques (for hyperthermia). Withdrawal manifests primarily as depression, difficulty concentrating, and somnolence (cocaine washout syndrome).

Most cocaine users are episodic recreational users. However, about 25% (or more) of users meet criteria for abuse or dependence. Use among adolescents has declined recently. Availability of highly biologically active forms, such as crack cocaine, has worsened the problem of cocaine dependence. Most cocaine in the US is about 50 to 60% pure; it may contain a wide array of fillers, adulterants, and contaminants.

Most cocaine in the US is volatilized and inhaled, but it may be snorted, or injected IV. For inhalation, the powdered hydrochloride salt is converted to a more volatile form, usually by adding $NaHCO_3$, water, and heat. The resultant precipitate (crack cocaine) is volatilized by heating (it is not burned) and inhaled. Onset of effect is quick, and intensity of the high rivals IV injection. Tolerance to cocaine occurs, and withdrawal from heavy use is characterized by somnolence, difficulty concentrating, increased appetite, and depression. The tendency to continue taking the drug is strong after a period of withdrawal.

Pathophysiology

Cocaine, an alkaloid present in the leaves of the coca plant, enhances norepinephrine, dopamine, and serotonin activity in the central and peripheral nervous systems.

Enhancement of dopamine activity is the likely cause of the drug's intended effects and thus of the reinforcement that contributes to developing abuse and dependence.

Norepinephrine activity accounts for the sympathomimetic effects: tachycardia, hypertension, mydriasis, diaphoresis, and hyperthermia.

Cocaine also blocks Na channels, accounting for its action as a local anesthetic. Cocaine causes vasoconstriction and thus can affect almost any organ. MI, cerebral ischemia and hemorrhage, aortic dissection, intestinal ischemia, and renal ischemia are possible sequelae.

Onset of cocaine's effects depends on mode of use:

- IV injection and smoking: Immediate onset, peak effect after about 3 to 5 min, and duration of about 15 to 20 min

- Intranasal use: Onset after about 3 to 5 min, peak effect at 20 to 30 min, and duration of about 45 to 90 min

- Oral use: Onset after about 10 min, peak effect at about 60 min, and duration of about 90 min

Because cocaine is such a short-acting drug, heavy users may inject it or smoke it repeatedly every 10 to 15 min.

Pregnancy: Use of cocaine during pregnancy can affect the fetus; the rate of placental abruption and spontaneous abortion is higher (see p. 2799).

Symptoms and Signs

Acute effects: Effects may differ depending on mode of use. When injected or smoked, cocaine causes hyperstimulation, alertness, euphoria, a sense of increased energy, and feelings of competence and power. The excitation and high are similar to those produced by injecting amphetamine. These feelings are less intense and disruptive in users who snort cocaine powder.

Users who smoke the drug may develop pneumothorax or pneumomediastinum, causing chest pain, dyspnea, or both. Myocardial ischemia due to cocaine use may also cause chest pain ("cocaine chest pain"), but cocaine can also cause chest pain in the absence of myocardial ischemia; the mechanism is unclear. Arrhythmias and conduction abnormalities may occur. Cardiac effects may result in sudden death. Binges, often over several days, lead to an exhaustion syndrome, involving intense fatigue and need for sleep.

Toxicity or overdose: An overdose may cause severe anxiety, panic, agitation, aggression,

sleeplessness, hallucinations, paranoid delusions, impaired judgment, tremors, seizures, and delirium. Mydriasis and diaphoresis are apparent, and heart rate and BP are increased. Death may result from MI or arrhythmias.

Severe overdose causes a syndrome of acute psychosis (eg, schizophrenic-like symptoms), hypertension, hyperthermia, rhabdomyolysis, coagulopathy, renal failure, and seizures. Patients with extreme clinical toxicity may, on a genetic basis, have decreased (atypical) serum cholinesterase, an enzyme needed for clearance of cocaine.

The concurrent use of cocaine and alcohol produces a condensation product, cocaethylene, which has stimulant properties and may contribute to toxicity.

Chronic effects: Severe toxic effects occur in compulsive heavy users. Myocardial fibrosis, left ventricular hypertrophy, and cardiomyopathy can develop. Rarely, repeated snorting causes nasal septal perforation due to local ischemia. Cognitive impairment, including impaired attention and verbal memory, occurs in some heavy users. Users who inject cocaine are subject to the typical infectious complications (see p. 1510).

Withdrawal: The main symptoms are depression, difficulty concentrating, and somnolence (cocaine washout syndrome). Appetite is increased.

Diagnosis

• Clinical evaluation

Diagnosis is usually made clinically. Drug levels are not measured. The cocaine metabolite, benzoylecgonine, is part of most routine urine drug screens (see p. 1510).

Treatment

• IV benzodiazepines

• Avoidance of β-blockers

• Cooling for hyperthermia as needed

Toxicity or overdose: Treatment of mild cocaine intoxication is generally unnecessary because the drug is extremely short-acting. Benzodiazepines are the preferred initial treatment for most toxic effects, including CNS excitation and seizures, tachycardia, and hypertension. Lorazepam 2 to 3 mg IV q 5 min titrated to effect may be used. High doses and a continuous infusion may be required. Propofol infusion, with mechanical ventilation, may be used for resistant cases. Hypertension that does not respond to benzodiazepines is treated with IV nitrates (eg, nitroprusside) or phentolamine; β-blockers are not recommended because they allow continued α-adrenergic stimulation. Hyperthermia can be life threatening and should be managed aggressively with sedation plus evaporative cooling, ice packs, and maintenance of intravascular volume and urine flow with IV normal saline solution. Phenothiazines lower seizure threshold, and their anticholinergic effects can interfere with cooling; thus, they are not preferred for sedation. Occasionally, severely agitated patients must be pharmacologically paralyzed and mechanically ventilated to ameliorate acidosis, rhabdomyolysis, or multisystem dysfunction.

Cocaine-related chest pain is evaluated as for any other patient with potential myocardial ischemia or aortic dissection, with chest x-ray, serial ECG, and serum cardiac markers. As discussed above, β-blockers are contraindicated, and benzodiazepines are a first-line drug. If coronary vasodilation is required after benzodiazepines are given, nitrates are used, or phentolamine 1 to 5 mg IV given slowly can be considered.

Abuse: Heavy users and people who inject the drug IV or smoke it are most likely to become dependent. Light users and people who take the drug nasally or orally are at lower risk of becoming dependent. Stopping sustained use requires considerable assistance, and the depression that may result requires

close supervision and treatment. Many outpatient therapies, including support and self-help groups and cocaine hotlines, exist. Inpatient therapy is used primarily when it is required by physical or mental comorbidity or when outpatient therapy has repeatedly been unsuccessful.

For treatment of infants born to cocaine-addicted mothers, see Prenatal Drug Exposure on p. 2799.

Amphetamines

Amphetamines are sympathomimetic drugs with CNS stimulant and euphoriant properties whose toxic adverse effects include delirium, hypertension, seizures, and hyperthermia (which can cause rhabdomyolysis and renal failure). Toxicity is managed with supportive care, including IV benzodiazepines (for agitation, hypertension, and seizures) and cooling techniques (for hyperthermia). There is no stereotypical withdrawal syndrome.

The original drug in this class, amphetamine, has been modified by various substitutions on its phenyl ring, resulting in many variations, including methamphetamine, methylenedioxymethamphetamine (MDMA or Ecstasy), methylenedioxyethylamphetamine (MDEA), and numerous others.

Some amphetamines, including dextroamphetamine, methamphetamine, and the related methylphenidate, are widely used medically to treat attention-deficit hyperactivity disorder, obesity, and narcolepsy, thus creating a supply subject to diversion for illicit use. Methamphetamine is easily manufactured illicitly.

Pathophysiology

Amphetamines enhance release of catecholamines, increasing intrasynaptic levels of norepinephrine, dopamine, and serotonin. The resulting marked α- and β-receptor stimulation and general CNS excitation account for the "desired" effects of increased alertness, euphoria, and anorexia, as well as the adverse effects of delirium, hypertension, hyperthermia, and seizures. Effects of amphetamines are similar, varying in intensity and duration of psychoactive effects; MDMA and its relatives have more mood-enhancing properties, perhaps related to a greater effect on serotonin. Amphetamines can be taken orally as pills or capsules, nasally by inhaling or smoking, or by injection.

Chronic effects: Repeated use of amphetamines induces dependence. Tolerance develops slowly, but amounts several 100-fold greater than the amount originally used may eventually be ingested or injected. Tolerance to various effects develops unequally. Tachycardia and increased alertness diminish, but hallucinations and delusions may occur.

Amphetamines typically cause erectile dysfunction in men but enhance sexual desire. Use is associated with unsafe sex practices, and users are at increased risk of sexually transmitted infections, including HIV infection. Amphetamine abusers are prone to injury because the drug produces excitation and grandiosity followed by excess fatigue and sleepiness.

Symptoms and Signs

Acute effects: Many psychologic effects of amphetamines are similar to those of cocaine; they include increased alertness and concentration, euphoria, and feelings of well-being and grandiosity. Palpitations, tremor, diaphoresis, and mydriasis may also occur during intoxication.

Binges (perhaps over several days) lead to an exhaustion syndrome, involving intense fatigue and need for sleep after the stimulation phase.

Toxicity or overdose: Tachycardia, arrhythmias, chest pain, hypertension, dizziness, nausea, vomiting, and diarrhea can occur. CNS effects include acute delirium and toxic psychosis. Overdose can also cause stroke (usually hemorrhagic), seizures, muscle rigidity, and hyperthermia (> 40° C); all of these effects may precipitate rhabdomyolysis, which can lead to renal failure.

Chronic effects: A paranoid psychosis may result from long-term use; rarely, the psychosis is precipitated by a single high dose or by repeated moderate doses. Typical features include delusions of

persecution, ideas of reference (notions that everyday occurrences have special meaning or significance personally meant for or directed to the patient), and feelings of omnipotence. Some users experience a prolonged depression, during which suicide is possible. Recovery from even prolonged amphetamine psychosis is usual but is slow. The more florid symptoms fade within a few days or weeks, but some confusion, memory loss, and delusional ideas commonly persist for months.

Users have a high rate of severe tooth decay affecting multiple teeth; causes include decreased salivation, acidic combustion products, and poor oral hygiene.

Withdrawal: Although no stereotypical withdrawal syndrome occurs when amphetamines are stopped, EEG changes occur, considered by some experts to fulfill the physical criteria for dependence. Abruptly stopping use may uncover or exacerbate underlying depression or precipitate a serious depressive reaction. Withdrawal is often followed by 2 or 3 days of intense fatigue or sleepiness and depression.

Diagnosis

• Clinical evaluation

• Testing as needed to exclude serious nondrug-related disorders (eg, causing altered mental status)

Diagnosis is usually made clinically, although when history of drug use and the diagnosis are unclear, tests are done as indicated for the undifferentiated patient with altered mental status, hyperpyrexia, or seizures. Evaluation then typically includes CT, lumbar puncture, and laboratory tests to identify infections and metabolic abnormalities. Amphetamines are usually part of routine urine drug screens (see p. 1510), which are done unless history of ingestion is clear; specific drug levels are not measured. Immunoassay urine screening tests for amphetamines may produce false-positive results and may not detect methamphetamine and methylphenidate.

Treatment

• IV benzodiazepines

• IV nitrates for hypertension unresponsive to benzodiazepines as needed

• Cooling for hyperthermia as needed

Toxicity or overdose: When significant oral toxicity is recent (eg, < 1 to 2 h), activated charcoal may be given to limit absorption, although this intervention has not been shown to reduce morbidity or mortality. Urinary acidification hastens amphetamine excretion, but it may worsen myoglobin precipitation in the renal tubules and thus is not recommended.

Benzodiazepines are the preferred initial treatment for CNS excitation, seizures, tachycardia, and hypertension. Lorazepam 2 to 3 mg IV q 5 min titrated to effect may be used. High doses or a continuous infusion may be required. Propofol, with mechanical ventilation, may be required for severe agitation. Hypertension that does not respond to benzodiazepines is treated with nitrates (occasionally nitroprusside) or other antihypertensives as needed, depending on the severity of the hypertension. β-Blockers (eg, metoprolol 2 to 5 mg IV) may be used for severe ventricular arrhythmias or tachycardia.

Hyperthermia can be life threatening and should be managed aggressively with sedation plus evaporative cooling, ice packs, and maintenance of intravascular volume and urine flow with IV normal saline solution.

Phenothiazines lower seizure threshold, and their anticholinergic effects can interfere with cooling; thus, they are not preferred for sedation.

Withdrawal and rehabilitation: No specific treatment is needed. BP and mood should be monitored initially. Patients whose depression persists for more than a brief period after amphetamines are stopped may respond to antidepressants.

Cognitive-behavioral therapy (a form of psychotherapy) is effective in some patients. There are no other proven treatments for rehabilitation and maintenance after detoxification.

Methylenedioxymethamphetamine (Ecstasy, MDMA)

MDMA (3,4-Methylenedioxymethamphetamine) is an amphetamine analog with stimulant and hallucinogenic effects.

MDMA acts primarily on neurons that produce and release serotonin, but it also affects dopaminergic neurons. MDMA is usually taken as a pill; effects begin 30 to 60 min after ingestion and typically last 4 to 6 h. MDMA is often used at dance clubs, concerts, and rave parties.

Symptoms and Signs

MDMA causes a state of excitement and disinhibition and accentuates physical sensation, empathy, and feelings of interpersonal closeness. Toxic effects are similar to those of the other amphetamines but are less common, perhaps because use is more likely to be intermittent. However, even with casual use, significant problems such as hyperthermia and centrally mediated hyponatremia may occur. The effects of intermittent, occasional use are uncertain. Rarely, fulminant hepatic failure occurs.

Chronic, repeated use may cause problems similar to those of amphetamines, including dependence. Some users develop paranoid psychosis. Cognitive decline may also occur with repeated, frequent use.

Diagnosis

MDMA may not be detected by routine urine immunoassay drug screens.

Treatment

Treatment for acute toxicity and dependency is similar to that for amphetamines, although treatment for acute overdose is less commonly needed.

Hallucinogens

Hallucinogens are a diverse group of drugs that can cause highly unpredictable, idiosyncratic reactions. Intoxication typically causes hallucinations, with altered perception, impaired judgment, ideas of reference, and depersonalization. There is no stereotypical withdrawal syndrome. Diagnosis is clinical. Treatment is supportive.

Traditional hallucinogens include lysergic acid diethylamide (LSD), psilocybin, and mescaline. All are derived from natural products:

- LSD from a fungus that often contaminates wheat and rye flour
- Psilocybin from several types of mushrooms
- Mescaline from the peyote cactus

Dozens of newer synthetic compounds ("designer drugs") have been produced, usually based on tryptamine or phenylethylamine molecules. Tryptamines include *N,N*-dimethyltryptamine (DMT) and 5-methoxy-*N,N*-diisopropyltryptamine (5-MeO-DIPT).

To complicate matters, many illicit drugs sold under one name actually contain another drug of abuse —often ketamine or phencyclidine (PCP), anesthetic drugs, dextromethorphan, or other drugs.

Some other drugs, including marijuana, also have hallucinogenic properties. The term hallucinogen persists, although use of these drugs may not cause hallucinations. Alternative terms, such as psychedelic and psychotomimetic, are even less appropriate.

Pathophysiology

LSD, psilocybin, and many designer hallucinogens are serotonin receptor agonists. For mescaline, a phenylethylamine similar to amphetamines, the exact mechanism has not been determined.

Mode of use and effects vary:

- LSD is taken orally from drug-impregnated blotter paper or as tablets. Onset of action is usually 30 to 60 min after ingestion; duration of effects can be 12 to 24 h.

- Psilocybin is taken orally; effects usually last about 4 to 6 h.

- Mescaline is taken orally as peyote buttons. Onset of effects is usually 30 to 90 min after ingestion; duration of effects is about 12 h.

- DMT, when smoked, has onset in 2 to 5 min; duration of effects is 20 to 60 min (accounting for its street name, "businessman's lunch").

A high degree of tolerance for LSD develops and disappears rapidly. Users tolerant of any of these drugs are cross-tolerant of the other drugs. Psychologic dependence varies greatly; there is no evidence of physical dependence or a withdrawal syndrome.

Symptoms and Signs

Intoxication results in altered perceptions, including synesthesias (eg, seeing sounds, hearing colors), intensification of sensations, enhanced empathy, depersonalization (feeling the self is not real), a distorted sense of the environment's reality, and changes in mood (usually euphoric, sometimes depressive). Users often refer to the combination of these effects as a trip. Periods of intense psychologic effects may alternate with periods of lucidity. LSD may also have several physical effects, including mydriasis, blurred vision, sweating, palpitations, and impaired coordination. Many other hallucinogens cause nausea and vomiting. With all, judgment is impaired.

Responses to hallucinogens depend on several factors, including the user's expectations, ability to cope with perceptual distortions, and the setting. With LSD, delusions and true hallucinations occur but are rare, as are anxiety attacks, extreme apprehensiveness, and panic states. Psilocybin and mescaline are more likely to cause hallucinations. When hallucinogenic reactions occur, they usually subside quickly if treated appropriately in a secure setting. However, some people (especially after using LSD) remain disturbed and may have a persistent psychotic state. Whether drug use has precipitated or uncovered preexisting psychotic potential or can cause this state in previously stable people is unclear.

Some people, especially long-term or repeat users (particularly of LSD), experience apparent drug effects long after they have stopped drug use. These episodes (flashbacks) are usually visual illusions but can include distortions of virtually any sensation (including self-image or perceptions of time or space) and hallucinations. Flashbacks can be precipitated by use of marijuana, alcohol, or barbiturates or by stress or fatigue or can occur without apparent reason. Mechanisms are not known. Flashbacks tend to subside within 6 to 12 mo.

Diagnosis

- Clinical evaluation

Diagnosis is usually made clinically. Drug levels are not measured. Except for PCP, most hallucinogens are not included in routine urine drug screens (see p. 1510).

Treatment

- For acute intoxication, supportive measures and relief of anxiety

• For persistent psychosis, psychiatric care

A quiet, calming environment with reassurance that the bizarre thoughts, visions, and sounds are due to the drug and will go away soon usually suffices. Anxiolytics (eg, lorazepam, diazepam) may help reduce severe anxiety.

Persistent psychotic states or other mental disorders require appropriate psychiatric care. Flashbacks that are transient or not unduly distressing to the patient require no special treatment. However, flashbacks associated with anxiety and depression may require anxiolytics as for acute adverse reactions.

Ketamine and Phencyclidine

Ketamine and phencyclidine are related drugs that can cause intoxication, sometimes with confusion or a catatonic state. Overdose can cause coma and, rarely, death.

Ketamine and phencyclidine (PCP) are chemically related anesthetics. These drugs are often used to adulterate or pass for other hallucinogens such as LSD.

Ketamine is available in liquid or powder form. When used illicitly, the powder form is typically snorted but can be taken orally. The liquid form is taken IV, IM, or sc.

PCP, once common, is no longer being legally manufactured. It is illegally manufactured and sold on the street under names such as angel dust; it is sometimes sold in combination with marijuana.

Symptoms and Signs

Intoxication, characterized by a giddy euphoria, occurs with lower doses; euphoria is often followed by bursts of anxiety or mood lability. Overdose causes a withdrawn state of depersonalization and disassociation; when doses are higher still, disassociation can become severe (known as a k-hole), with combativeness, ataxia, dysarthria, muscular hypertonicity, nystagmus, hyperreflexia, and myoclonic jerks. With very high doses, acidosis, hyperthermia, tachycardia, severe hypertension, seizures, and coma may occur; deaths are unusual. Acute effects generally fade after 30 min.

Diagnosis

• Clinical evaluation

Diagnosis is usually clinical. Ketamine is not detected by routine urine drug screens; high-performance liquid chromatography testing must be requested when ketamine use must be confirmed.

Treatment

• Supportive measures

Patients should be kept in a quiet, calming environment and closely observed. Benzodiazepines can be used to manage seizures. Further treatment is rarely needed.

Volatile Nitrites

Nitrites (poppers, as amyl, butyl, or isobutyl nitrite, sold with street names such as Locker Room and Rush) may be inhaled to enhance sexual pleasure. There is little evidence of significant risk, although nitrites and nitrates cause vasodilation, with brief hypotension, dizziness, and flushing, followed by reflex tachycardia (see Table 340-8 on p. 3345). Nitrites may cause methemoglobinemia. However, they are dangerous when combined with drugs used for erectile enhancement; the combination can lead to severe hypotension and death.

Volatile Solvents

Inhalation of volatile industrial solvents and solvents from aerosol sprays can cause a state of intoxication. Chronic use can result in neuropathies and hepatotoxicity.

Use of volatile solvents (eg, acetates, alcohol, chloroform, ether, aliphatic and aromatic hydrocarbons, chlorinated hydrocarbons, ketones) continues to be an endemic problem among adolescents. Common commercial products (eg, glues and adhesives, paints, cleaning fluids) contain these substances; thus, children and adolescents can easily obtain them. About 10% of adolescents in the US have reportedly inhaled volatile solvents.

Volatile solvents temporarily stimulate the CNS before depressing it. Partial tolerance and psychologic dependence develop with frequent use, but a withdrawal syndrome does not occur.

Symptoms and Signs

Acute symptoms of dizziness, drowsiness, slurred speech, and unsteady gait occur early. Impulsiveness, excitement, and irritability may occur. As effects on the CNS increase, illusions, hallucinations, and delusions develop. Users experience a euphoric, dreamy high, culminating in a short period of sleep. Delirium with confusion, psychomotor clumsiness, emotional lability, and impaired thinking develop. The intoxicated state may last from minutes to > 1 h.

Sudden death can result from respiratory arrest or airway occlusion due to CNS depression or arrhythmias (perhaps due to myocardial sensitization).

Complications of chronic use may result from the effect of the solvent or from other toxic ingredients (eg, lead in gasoline). Carbon tetrachloride may cause a syndrome of hepatic and renal failure. Toluene may cause degeneration of CNS white matter. Injuries to brain, peripheral nerves, liver, kidneys, and bone marrow may result from heavy exposure or hypersensitivity.

Diagnosis

Volatile solvents are not detected by routine drug screens.

Treatment

Treatment of solvent-dependent adolescents is difficult, and relapse is frequent. However, most users stop solvent use by the end of adolescence. Intensive attempts to broadly improve patients' social skills and status in family, school, and society may help. For symptoms and treatment of poisoning with specific solvents, see Table 340-8 on p. 3345.

Gamma Hydroxybutyrate

Gamma hydroxybutyrate causes intoxication resembling alcohol or ketamine intoxication and, especially when combined with alcohol, can lead to respiratory depression, seizures, and rarely death.

Gamma hydroxybutyrate (GHB, also called "G") is similar to the neurotransmitter γ-aminobutyric acid (GABA), but it can cross the blood-brain barrier and so can be taken by mouth. It is similar to ketamine in its effects but lasts longer and is far more dangerous.

GHB produces feelings of relaxation and tranquility. It may also cause fatigue and disinhibition. At higher doses, GHB may cause dizziness, loss of coordination, nausea, and vomiting. Coma and respiratory depression may also occur. Combining GHB and any other sedative, especially alcohol, is extremely dangerous. Most deaths have occurred when GHB was taken with alcohol.

Withdrawal symptoms occur if GHB is not taken for several days after previous frequent use.

Treatment is directed at symptoms. Mechanical ventilation may be needed if breathing is affected. Most

people recover rapidly, although effects may not fade for 1 to 2 h.

Anabolic Steroids

Anabolic steroids are often used to enhance physical performance and promote muscle growth. When used inappropriately, chronically at high doses and without medical supervision, they can cause erratic and irrational behavior and a wide range of physical adverse effects.

Anabolic steroids include testosterone and any drugs chemically and pharmacologically related to testosterone that promote muscle growth; numerous drugs are available. Anabolic steroids are used clinically to treat low testosterone levels (see Male Hypogonadism on p. 2340). Additionally, because anabolic steroids are anticatabolic and improve protein utilization, they are sometimes given to burn, bedbound, or other debilitated patients to prevent muscle wasting. Some physicians prescribe them to patients with AIDS-related wasting or with cancer. However, there are few data to recommend such therapy and little guidance on how supplemental androgens may affect underlying disorders. Testosterone has been reputed to benefit wound healing and muscle injury, although few data support these claims.

Anabolic steroids are used illicitly to increase lean muscle mass and strength; resistance training and a certain diet can enhance these effects. There is no direct evidence that anabolic steroids increase endurance or speed, but substantial anecdotal evidence suggests that athletes taking them can perform more frequent high-intensity workouts. Muscle hypertrophy is unequivocal.

Estimates of lifetime incidence of anabolic steroid abuse range from 0.5 to 5% of the population, but subpopulations vary significantly (eg, higher rates for bodybuilders and competitive athletes). In the US, the reported rate of use is 6 to 11% among high school-aged males, including an unexpected number of nonathletes, and about 2.5% among high school-aged females.

Pathophysiology

Anabolic steroids have androgenic effects (eg, changes in hair or in libido, aggressiveness) and anabolic effects (eg, increased protein utilization, increased muscle mass). Androgenic effects cannot be separated from the anabolic, but some anabolic steroids have been synthesized to minimize the androgenic effects.

Testosterone is rapidly degraded by the liver; oral testosterone is inactivated too rapidly to be effective, and injectable testosterone must be modified (eg, by esterification) to retard absorption or delay breakdown. Analogs modified by 17α-alkylation are often effective orally, but adverse effects may be increased. Transdermal preparations are also available.

Chronic effects: Adverse effects vary significantly by dose and drug. There are few adverse effects at physiologic replacement doses (eg, methyltestosterone 10 to 50 mg/day or its equivalent). Athletes may use doses 10 to 50 times this range. At high doses, some effects are clear; others are equivocal (see Table 160-4). Uncertainties exist because most studies involve abusers who may not report doses accurately and who also use black market drugs, many of which are counterfeit and contain (despite labeling) varying doses and substances.

Athletes may take steroids for a certain period, stop, then start again (cycling) several times a year. Intermittently stopping the drugs is believed to allow endogenous testosterone levels, sperm count, and the hypothalamic-pituitary-gonadal axis to return to normal. Anecdotal evidence suggests that cycling may decrease harmful effects and the need for increasing drug doses to attain the desired effect.

Athletes frequently use many drugs simultaneously (a practice called stacking) and alternate routes of administration (oral, IM, or transdermal). Increasing the dose through a cycle (pyramiding) may result in doses 5 to 100 times the physiologic dose. Stacking and pyramiding are intended to increase receptor binding and minimize adverse effects, but these benefits have not been proved.

[**Table 160-4.** Adverse Effects of Anabolic Steroids]

Symptoms and Signs

The most characteristic sign is a rapid increase in muscle mass. The rate and extent of increase are directly related to the doses taken. Patients taking physiologic doses have slow and often unnoticeable growth; those taking megadoses may increase lean body weight by several pounds per month. Increases in energy level and libido (in men) occur but are more difficult to identify.

Psychologic effects (usually only with very high doses) are often noticed by family members:

• Wide and erratic mood swings

• Irrational behavior

• Increased aggressiveness ("roid rage")

• Irritability

• Increased libido

• Depression

Increased acne is common in both sexes; libido may increase or, less commonly, decrease; aggressiveness and appetite may increase. Gynecomastia, testicular atrophy, and decreased fertility may occur in males. Virilizing effects (eg, alopecia, enlarged clitoris, hirsutism, deepened voice) are common among females. Also, breast size may decrease; vaginal mucosa may atrophy; and menstruation may change or stop. Virilization and gynecomastia may be irreversible.

Diagnosis

• Urine testing

A urine screen usually identifies users of anabolic steroids. Metabolites of anabolic steroids can be detected in urine up to 6 mo (even longer for some types of anabolic steroids) after the drugs are stopped. Testosterone taken exogenously is indistinguishable from endogenous testosterone. However, if high levels of testosterone are detected, the ratio between testosterone and epitestosterone (an endogenous steroid that chemically is nearly identical to testosterone) is measured. Normally, the ratio is < 6:1; if exogenous testosterone is being used, the ratio is higher.

Treatment

• Cessation of use

The main treatment is cessation of use. Although physical dependence does not occur, psychologic dependence, particularly in competitive bodybuilders, may exist. Gynecomastia may require surgical reduction.

Prevention

Physicians caring for adolescents and young adults should be alert to the signs of steroid abuse and teach patients about its risks. Education about anabolic steroids should start by the beginning of middle school. Use of programs that teach alternative, healthy ways to increase muscle size and improve performance through good nutrition and weight training techniques may help.

Substance Use in Children and Adolescents

Substance use is common among children, especially adolescents. Regardless of economic or ethnic background, alcohol, tobacco, and marijuana are consistently the most commonly used substances. Use of other substances, including amphetamines and methamphetamines, inhalants, hallucinogens, cocaine,

anabolic steroids, opioids, and so-called date rape drugs and club drugs (eg, methylenedioxymethamphetamine [MDMA], ketamine, gamma hydroxybutyrate), is less common, and the prevalence of use of each varies more over time. Of growing concern is a reported increase in the prevalence of prescription opioid abuse.

Children and adolescents use drugs for a variety of reasons. Some do so to escape from perceived pressures (eg, parental pressure, societal pressure) or to challenge authority; others are disposed to novelty seeking and risk taking. Influence of peers and the media's portrayal of substances such as alcohol are other commonly cited reasons. Poor self-control, lack of parental monitoring, or various psychologic disorders (eg, conduct disorder, attention-deficit/hyperactivity disorder, depression) may increase risk. Parental attitudes and the examples that parents set in their own use of alcohol, tobacco, prescription drugs, and other substances are a powerful influence.

Diagnosis

• Screening

Primary care physicians should be prepared to screen their adolescent patients for use of alcohol and drinking and provide counseling and, when necessary, referral to other treatment services and resources. The CRAFFT questionnaire is one validated screening tool. Patients with ≥ 2 positive answers require further evaluation. Physicians ask patients whether they do or have done the following:

• C: Ride in a *C*ar driven by someone (including themselves) who is "high" or has been drinking alcohol or using drugs

• R: Drink alcohol or use drugs to *R*elax, feel better about themselves, or fit in

• A: Drink alcohol or use drugs while they are *A*lone

• F: *F*orget things they did while drinking or using drugs

• F: Are ever told by family members or *F*riends that they should drink or use drugs less

• T: Get into *T*rouble while drinking or using drugs

Chapter 161. Eating Disorders

Introduction

Eating disorders are grouped into 3 categories: anorexia nervosa, bulimia nervosa, and eating disorder not otherwise specified (EDNOS). Within EDNOS, provisional diagnostic criteria are provided for binge eating disorder.

Anorexia Nervosa

Anorexia nervosa is characterized by a relentless pursuit of thinness, a morbid fear of obesity, a refusal to maintain a minimally normal body weight, resulting in body weight below the normal range and, in women, amenorrhea. Diagnosis is clinical. Most treatment is with some form of psychologic therapy. Olanzapine may help with weight gain.

Anorexia nervosa occurs predominantly in girls and young women. Onset is usually during adolescence.

The exact etiology is unknown. Other than being female, few risk factors have been identified. In Western society, obesity is considered unattractive and unhealthy, and the desire to be thin is pervasive, even among children. More than 50% of prepubertal girls diet or take other measures to control their weight. Excessive concern about weight or a history of dieting appears to indicate increased risk, and some genetic predisposition probably exists. Studies of identical twins have shown a concordance of < 50%. Family and social factors probably play a role. Many patients belong to middle or upper socioeconomic classes; are meticulous, compulsive, and intelligent; and have very high standards for achievement and success.

Two types of anorexia nervosa are recognized:

- Restricting type: Patients restrict food intake but do not regularly engage in binge eating or purging behavior.

- Binge-eating/purging type: Patients regularly binge, then induce vomiting, misuse laxatives, diuretics, or enemas, or a combination.

Binges are defined as consumption of a much larger amount of food than most people would eat in a similar time period under similar circumstances with loss of control, ie, perceived inability to resist or stop eating.

Pathophysiology

Endocrine abnormalities are common; they include low levels of luteinizing hormone (decreased secretion), low levels of thyroxine (T_4) and triiodothyronine (T_3), and increased cortisol secretion. Menses usually cease. Bone mass declines. In severely undernourished patients, virtually every major organ system may malfunction.

Dehydration and metabolic alkalosis may occur, and serum K may be low; all are aggravated by induced vomiting and laxative or diuretic use.

Cardiac muscle mass, chamber size, and output decrease; mitral valve prolapse is commonly detected. Some patients have prolonged QT intervals (even when corrected for heart rate), which, with the risks imposed by electrolyte disturbances, may predispose to tachyarrhythmias. Sudden death, most likely due to ventricular tachyarrhythmias, may occur.

Symptoms and Signs

Anorexia nervosa may be mild and transient or severe and long-standing. Most patients are lean yet are concerned about body weight and restrict food intake. Preoccupation and anxiety about weight increase,

even as emaciation develops.

Anorexia is a misnomer because appetite remains until patients become cachectic. Patients are preoccupied with food:

• They study diets and calories.

• They hoard, conceal, and waste food.

• They collect recipes.

• They prepare elaborate meals for other people.

Patients are often manipulative, lying about food intake and concealing behavior, such as induced vomiting. Binge-eating/purging occurs in 30 to 50% of patients. The others simply restrict their food intake.

Many anorectics also exercise excessively to control weight. Even patients who appear cachectic tend to remain very active (including pursuing vigorous exercise programs), are free of symptoms of nutritional deficiencies, and have no unusual susceptibility to infections.

Reports of bloating, abdominal distress, and constipation are common. Patients usually lose interest in sex. Depression occurs frequently.

Common physical findings include bradycardia, low BP, hypothermia, lanugo hair or slight hirsutism, and edema. Body fat is usually greatly reduced. Patients who vomit frequently may have eroded dental enamel, painless salivary gland enlargement, and an inflamed esophagus.

Diagnosis

• Clinical criteria

Denial is a prominent feature, and patients resist evaluation and treatment. They are usually brought to the physician's attention by family members or by intercurrent illness.

Clinical characteristics include the following:

• Body weight ≤ 85% of expected weight (with a BMI of < 17.5 kg/m^2)

• Fear of obesity

• Denial of illness (body image disturbance)

• Amenorrhea in females

Patients should otherwise appear well. The key to diagnosis is eliciting the central fear of fatness, which is not diminished by weight loss.

Differential diagnosis: Another mental disorder, such as schizophrenia or primary depression, may cause similar findings.

Rarely, a severe physical disorder may cause substantial weight loss. Disorders to consider include malabsorption syndromes (eg, due to inflammatory bowel disease or celiac sprue), new-onset type 1 diabetes, adrenal insufficiency, and CNS tumors. Amphetamine abuse may cause similar symptoms.

Prognosis

Without treatment, mortality rates approach 10%; unrecognized mild disease probably rarely leads to

death. With treatment, one half of patients regain most or all of lost weight and reverse any endocrine and other complications. About one fourth have intermediate outcomes and may relapse. The remaining one fourth have a poor outcome, including relapses and persistent physical and mental complications.

Treatment

• Nutrition supplementation

• Psychologic therapy (eg, cognitive-behavioral treatment)

• For adolescents, family therapy

Treatment may require life-saving short-term intervention to restore body weight. When weight loss has been severe or rapid or when weight has fallen below about 75% of ideal, prompt restoration of weight becomes critical, and hospitalization should be considered. If any doubt exists, patients should be hospitalized. Removing patients from their home sometimes reverses a downhill course, but psychiatric treatment is also required.

Nutritional therapy, which begins by providing about 30 to 40 kcal/kg/day, can produce weight gains of up to 1.5 kg/wk during inpatient care and 0.5 kg/wk during outpatient care. Oral feedings are best, but very resistant, undernourished patients occasionally require nasogastric feedings. Loss of bone mass should be treated with elemental Ca 1200 to 1500 mg/day, vitamin D 600 to 800 IU/day, and, if severe, a bisphosphonate.

Once nutritional, fluid, and electrolyte status has been stabilized, long-term treatment begins. Outpatient psychologic therapy is the cornerstone of treatment. Cognitive-behavioral therapy is the modality of choice, done over a period of 1 yr for weight-restored patients and up to 2 yr for low-weight patients. Results are best in adolescents who have had the disorder < 6 mo. Family therapy, particularly using the Maudsley model, is useful for adolescents. This model has 3 phases:

• Family members are taught how to refeed the adolescent (eg, through a supervised family meal) and thus restore the adolescent's weight (in contrast to many approaches, this model does not assign blame to the family or the adolescent).

• Control over eating is gradually returned to the adolescent.

• After the adolescent is able to maintain the restored weight, therapy focuses on engendering a healthy adolescent identity.

Treatment is complicated by patients' abhorrence of weight gain, denial of illness, and manipulative behavior. The physician should attempt to provide a calm, concerned, stable relationship while encouraging a reasonable caloric intake.

Although psychologic therapy is primary, drugs are sometimes used. Second-generation antipsychotics (eg, olanzapine 10 mg po once/day) may help produce weight gain and relieve the morbid fear of obesity. Fluoxetine, beginning with 20 mg once/day, may help prevent relapse after weight has been restored.

Bulimia Nervosa

Bulimia nervosa is characterized by recurrent episodes of binge eating followed by some form of excessive compensatory behavior such as purging (self-induced vomiting, laxative or diuretic abuse), fasting, or driven exercise occurring at least 2 times/wk for 3 mo. Diagnosis is based on history and examination. Treatment is with psychologic therapy and antidepressants.

Bulimia nervosa affects about 1.6% of adolescent and young women and 0.5% of men of comparable age. Those affected are persistently and overly concerned about body shape and weight. Unlike patients with anorexia nervosa, those with bulimia nervosa are usually of normal weight.

Pathophysiology

Serious fluid and electrolyte disturbances, especially hypokalemia, occur occasionally. Very rarely, the stomach ruptures or the esophagus is torn during a binge, leading to life-threatening complications.

Because substantial weight loss does not occur, the serious nutritional deficiencies that occur with anorexia nervosa are not present. Cardiomyopathy may result from long-term abuse of syrup of ipecac to induce vomiting.

Symptoms and Signs

Patients typically describe binge-purge behavior. Binges involve rapid consumption of an amount of food definitely larger than most people would eat in a similar period of time under similar circumstances accompanied by feelings of loss of control.

Patients tend to consume high-calorie foods (eg, ice cream, cake). The amount of food consumed in a binge varies, sometimes involving thousands of calories. Binges tend to be episodic, are often triggered by psychosocial stress, may occur as often as several times a day, and are carried out in secret.

Binging is followed by purging: self-induced vomiting, use of laxatives or diuretics, excessive exercise, or fasting.

Patients are typically of normal weight; a minority is overweight or obese. Most symptoms and physical complications result from purging. Self-induced vomiting leads to erosion of dental enamel of the front teeth, painless parotid (salivary) gland enlargement, and an inflamed esophagus. Danger signs include

- Swollen parotid glands
- Scars on the knuckles (from induced vomiting)
- Dental erosion

Patients with bulimia nervosa tend to be more aware of and remorseful or guilty about their behavior than those with anorexia nervosa and are more likely to acknowledge their concerns when questioned by a sympathetic physician. They also appear less introverted and more prone to impulsive behavior, drug and alcohol abuse, and overt depression.

Diagnosis

- Clinical criteria

Criteria for diagnosis include the following:

- Recurrent binge eating (the uncontrolled consumption of unusually large amounts of food) at least twice/wk for 3 mo
- Recurrent inappropriate compensatory behavior to influence body weight (at least twice/wk for 3 mo)
- Self-evaluation unduly influenced by body shape and weight concerns

Treatment

- Cognitive-behavioral therapy (CBT)
- Interpersonal psychotherapy (IPT)
- SSRIs

CBT is the treatment of choice. Therapy usually involves 16 to 20 individual sessions over 4 to 5 mo, although it can also be done as group therapy. Treatment aims to increase motivation for change, replace dysfunctional dieting with a regular and flexible pattern of eating, decrease undue concern with body shape and weight, and prevent relapse. CBT eliminates binge eating and purging in about 30% to 50% of patients. Many others show improvement; some drop out of treatment or do not respond. Improvement is usually well-maintained over the long-term.

In IPT, the emphasis is on helping patients identify and alter current interpersonal problems that may be maintaining the eating disorder. The treatment is both nondirective and noninterpretive and does not focus directly on eating disorder symptoms. IPT can be considered an alternative when CBT is unavailable.

SSRIs used alone reduce the frequency of binge eating and vomiting, although long-term outcomes are unknown. SSRIs are also effective in treating comorbid anxiety and depression.

Binge Eating Disorder

Binge eating disorder is characterized by recurrent episodes of consuming large amounts of food with a feeling of loss of control. It is not followed by inappropriate compensatory behavior, such as self-induced vomiting or laxative abuse. Diagnosis is clinical.

Binge eating disorder affects about 3.5% of women and 2.0% of men in the general population. Unlike bulimia nervosa, binge eating disorder occurs most commonly among obese people and contributes to excessive caloric intake; it may be present in ≥ 30% of patients in some weight reduction programs. Compared with people with anorexia nervosa or bulimia nervosa, those with binge eating disorder are older and more likely to be men.

People with binge eating disorder are usually distressed by it, especially if they are trying to lose weight. Clinical depression and preoccupation with body shape, weight, or both are more common in obese people with binge eating disorder than in obese people who are not binge eaters.

Diagnosis

• Clinical criteria

Diagnosis requires binge eating for 2 days/wk for at least 6 mo and a sense of lack of control over eating, according to research criteria in the *Diagnostic and Statistical Manual of Mental Disorders* , Fourth Edition Text Revision. Other criteria include presence of ≥ 3 of the following:

• Eating much more rapidly than normal

• Eating until feeling uncomfortably full

• Eating large amounts of food when not feeling physically hungry

• Eating alone because of embarrassment

• Feeling disgusted, depressed, or guilty after overeating

Treatment

• Cognitive-behavioral therapy (CBT)

• Sometimes interpersonal psychotherapy (IPT)

• Consideration of drug therapy with SSRIs or sibutramine

CBT is the most researched and best supported treatment. IPT and dialectical behavior therapy may also

be effective. Both CBT and IPT result in remission rates of ≥ 60%; improvement is usually well-maintained over the long-term. These treatments do not produce significant weight loss in obese patients.

Conventional behavioral weight loss treatment has short-term effectiveness in reducing binge eating, but patients tend to relapse. Antidepressant drugs also have short-term effectiveness in eliminating binge eating, but long-term effectiveness is unknown. Initial results with the appetite-suppressing drug sibutramine are promising.

Chapter 162. Mood Disorders

Introduction

(For mood disorders in children, see p. 3055.)

Mood disorders are emotional disturbances consisting of prolonged periods of excessive sadness, excessive joyousness, or both. Mood disorders are categorized as depressive or bipolar. Anxiety and related disorders (see p. 1493) also affect mood.

Sadness and joy (elation) are part of everyday life. Sadness is a universal response to defeat, disappointment, and other discouraging situations. Joy is a universal response to success, achievement, and other encouraging situations. Grief, a form of sadness, is considered a normal emotional response to a loss. Bereavement refers specifically to the emotional response to death of a loved one.

A mood disorder is diagnosed when sadness or elation is overly intense and persistent and is accompanied by a requisite number of other mood disorder symptoms. In such cases, intense sadness is termed depression, and intense elation is termed mania. Depressive disorders are characterized by depression; bipolar disorders are characterized by varying combinations of depression and mania.

Lifetime risk of suicide (see p. 1579) for people with a depressive disorder is 2 to 15%, depending on severity of the disorder. Risk is further increased in the following cases:

• At the start of treatment, when psychomotor activity is returning to normal but mood is still dark

• During mixed bipolar states

• At personally significant anniversaries

• By severe anxiety

• By alcohol and substance use

Other complications include disability ranging from mild to complete inability to function, maintain social interaction, and participate in routine activities; impaired food intake; severe anxiety; alcoholism; and other drug dependencies.

Depressive Disorders

Depressive disorders are characterized by sadness severe enough or persistent enough to interfere with function and often by decreased interest or pleasure in activities. Exact cause is unknown but probably involves heredity, changes in neurotransmitter levels, altered neuroendocrine function, and psychosocial factors. Diagnosis is based on history. Treatment usually consists of drugs, psychotherapy, or both and sometimes electroconvulsive therapy.

The term depression is often used to refer to any of several depressive disorders. Three are classified in the *Diagnostic and Statistical Manual of Mental Disorders* , Fourth Edition Revision (DSM-IV-TR) by specific symptoms:

• Major depressive disorder (often called major depression)

• Dysthymia

• Depressive disorder not otherwise specified

Two others are classified by etiology:

• Depressive disorder due to a general physical condition

• Substance-induced depressive disorder

Depressive disorders occur at any age but typically develop during the mid teens, 20s, or 30s. In primary care settings, as many as 30% of patients report depressive symptoms, but < 10% have major depression.

The term depression is often used to describe the low or discouraged mood that results from disappointments or losses. However, a better term for such a mood is demoralization. The negative feelings of demoralization, unlike those of depression, resolve when circumstances or events improve; the low mood usually lasts days rather than weeks or months, and suicidal thoughts and prolonged loss of function are much less likely.

Etiology

Exact cause is unknown, but genetic and environmental factors contribute.

Heredity accounts for about half of the etiology (less so in late-onset depression). Thus, depression is more common among 1st-degree relatives of depressed patients, and concordance between identical twins is high. Also, genetic factors probably influence the development of depressive responses to adverse events.

Other theories focus on changes in neurotransmitter levels, including abnormal regulation of cholinergic, catecholaminergic (noradrenergic or dopaminergic), and serotonergic (5-hydroxytryptamine) neurotransmission. Neuroendocrine dysregulation may be a factor, with particular emphasis on 3 axes: hypothalamic-pituitary-adrenal, hypothalamic-pituitary-thyroid, and growth hormone.

Psychosocial factors also seem to be involved. Major life stresses, especially separations and losses, commonly precede episodes of major depression; however, such events do not usually cause lasting, severe depression except in people predisposed to a mood disorder.

People who have had an episode of major depression are at higher risk of subsequent episodes. People who are introverted and who have anxious tendencies may be more likely to develop a depressive disorder. Such people often do not develop the social skills to adjust to life pressures. Depression may also develop in people with other mental disorders.

Women are at higher risk, but no theory explains why. Possible factors include greater exposure to or heightened response to daily stresses, higher levels of monoamine oxidase (the enzyme that degrades neurotransmitters considered important for mood), higher rates of thyroid dysfunction, and endocrine changes that occur with menstruation and at menopause. In postpartum depression (see p. 2689), symptoms develop within 4 wk after delivery; endocrine changes have been implicated, but the specific cause is unknown.

In seasonal affective disorder, symptoms develop in a seasonal pattern, typically during autumn or winter; the disorder tends to occur in climates with long or severe winters.

Depressive symptoms or disorders may accompany various physical disorders, including thyroid and adrenal gland disorders, benign and malignant brain tumors, stroke, AIDS, Parkinson's disease, and multiple sclerosis (see Table 162-1). Certain drugs, such as corticosteroids, some β-blockers, interferon, and reserpine, can also result in depressive disorders. Abuse of some recreational drugs (eg, alcohol, amphetamines) can lead to or accompany depression. Toxic effects or withdrawal of drugs may cause transient depressive symptoms.

Symptoms and Signs

Depression causes cognitive, psychomotor, and other types of dysfunction (eg, poor concentration,

fatigue, loss of sexual desire, loss of pleasure), as well as a depressed mood. Other mental symptoms or disorders (eg, anxiety and panic attacks) commonly coexist, sometimes complicating diagnosis and treatment.

Patients with all forms of depression are more likely to abuse alcohol or other recreational drugs in an attempt to self-treat sleep disturbances or anxiety symptoms; however, depression is a less common cause of alcoholism and drug abuse than was once thought. Patients are also more likely to become heavy smokers and to neglect their health, increasing the risk of development or progression of other disorders (eg, COPD).

[**Table 162-1.** Some Causes of Symptoms in Depression and Mania]

Depression may reduce protective immune responses. Depression increases risk of cardiovascular disorders, MIs, and stroke, perhaps because in depression, cytokines and factors that increase blood clotting are elevated and heart rate variability is decreased—all potential risk factors for cardiovascular disorders.

Major depression (unipolar disorder): Periods (episodes) that include ≥ 5 mental or physical symptoms and last ≥ 2 wk are classified as major depression. One of the symptoms must be sadness deep enough to be described as despondency or despair (often called depressed mood) or loss of interest or pleasure in usual activities (anhedonia). Other mental symptoms include feelings of worthlessness or guilt, recurrent thoughts of death or suicide, and a reduced ability to concentrate. Physical symptoms include changes in weight or appetite, loss of energy, fatigue, psychomotor retardation or agitation, and sleep disorders (eg, insomnia, hypersomnia, early morning awakening). Patients may appear miserable, with tearful eyes, furrowed brows, down-turned corners of the mouth, slumped posture, poor eye contact, lack of facial expression, little body movement, and speech changes (eg, soft voice, lack of prosody, use of monosyllabic words). Appearance may be confused with Parkinson's disease. In some patients, depressed mood is so deep that tears dry up; they report that they are unable to experience usual emotions and feel that the world has become colorless and lifeless. Nutrition may be severely impaired, requiring immediate intervention. Some depressed patients neglect personal hygiene or even their children, other loved ones, or pets.

Major depression is often divided into subgroups:

- **Psychotic:** This subgroup is characterized by delusions, often of having committed unpardonable sins or crimes, of harboring incurable or shameful disorders, or of being persecuted. Patients with delusions may also have auditory or visual hallucinations (eg, hearing accusatory or condemning voices). If only voices are described, careful consideration should be given to whether the voices represent true hallucinations.

- **Catatonic:** This subgroup is characterized by severe psychomotor retardation or excessive purposeless activity, withdrawal, and, in some patients, grimacing and mimicry of speech (echolalia) or movement (echopraxia).

- **Melancholic:** This subgroup is characterized by loss of pleasure in nearly all activities, inability to respond to pleasurable stimuli, unchanging emotional expression, excessive or inappropriate guilt, early morning awakening, marked psychomotor retardation or agitation, and significant anorexia or weight loss.

- **Atypical:** This subgroup is characterized by a brightened mood in response to positive events and rejection sensitivity, resulting in depressed overreaction to perceived criticism or rejection, feelings of leaden paralysis or anergy, weight gain or increased appetite, and hypersomnia. Symptoms tend to worsen as the day passes.

Dysthymia: Low-level or subthreshold depressive symptoms that persist for ≥ 2 yr are classified as dysthymia. Symptoms typically begin insidiously during adolescence and follow a low-grade course over many years or decades (diagnosis requires a course of ≥ 2 yr); dysthymia may intermittently be complicated by episodes of major depression. Affected patients are habitually gloomy, pessimistic,

humorless, passive, lethargic, introverted, hypercritical of self and others, and complaining. Patients with chronic depressive states, whether dysthymia or chronic major depression, are also more likely to have underlying anxiety, substance use, or personality (ie, borderline personality) disorders.

Depression not otherwise specified (NOS): Clusters of symptoms that do not meet criteria for other depressive disorders are classified as depression NOS. For example, minor depressive disorder may involve ≥ 2 wk of any of the symptoms of major depression but fewer symptoms than the 5 required for diagnosing major depression. Brief depressive disorder involves the same symptoms required for diagnosing major depression but lasts only 2 days to 2 wk. Premenstrual dysphoric disorder involves a depressed mood, anxiety, and decreased interest in activities but only during most menstrual cycles, beginning in the luteal phase and ending within a few days after onset of menses.

Mixed anxiety-depression: Although not considered a type of depression in DSM-IV-TR, this condition, also called anxious depression, refers to concurrent mild symptoms common to anxiety and depression. The course is usually chronically intermittent. Because depressive disorders are more serious, patients with mixed anxiety-depression should be treated for depression.

Diagnosis

- Clinical criteria (DSM-IV-TR)
- CBC, thyroid-stimulating hormone, vitamin B_{12}, and folate levels to rule out physical disorders that can cause depression

Diagnosis is based on identifying the symptoms and signs (see p. 1539). Several brief questionnaires are available for screening. They help elicit some depressive symptoms but cannot be used alone for diagnosis. Specific close-ended questions help determine whether patients have symptoms required by DSM-IV-TR criteria for diagnosis of major depression.

Severity is determined by the degree of pain and disability (physical, social, occupational) and by duration of symptoms. A physician should gently but directly ask patients about any thoughts and plans to harm themselves or others (see p. 1579). Psychosis and catatonia indicate severe depression. Melancholic features indicate severe or moderate depression. Coexisting physical conditions, substance abuse disorders, and anxiety disorders may add to severity.

Differential diagnosis: Depressive disorders must be distinguished from demoralization. Other mental disorders (eg, anxiety disorders) can mimic or obscure the diagnosis of depression. Sometimes more than one disorder is present. Major depression (unipolar disorder) must be distinguished from bipolar disorder (see p. 1548).

In elderly patients, depression can manifest as dementia of depression (formerly called pseudodementia), which causes many of the symptoms and signs of dementia such as psychomotor retardation and decreased concentration (see p. 1673). However, early dementia may cause depression. In general, when the diagnosis is uncertain, treatment of a depressive disorder should be tried.

Differentiating chronic depressive disorders, such as dysthymia, from substance abuse disorders may be difficult, particularly because they can coexist and may contribute to each other.

Physical disorders must also be excluded as a cause of depressive symptoms. Hypothyroidism often causes symptoms of depression and is common, particularly among the elderly. Parkinson's disease, in particular, may manifest with symptoms that mimic depression (eg, loss of energy, lack of expression, paucity of movement). A thorough neurologic examination is needed to exclude this disorder.

Testing: No laboratory findings are pathognomonic for depressive disorders. Tests for limbic-diencephalic dysfunction are rarely indicated or helpful. However, laboratory testing is necessary to exclude physical conditions that can cause depression. Tests include CBC, TSH levels, and routine electrolyte, vitamin B_{12}, and folate levels. Testing for illicit drug use is sometimes appropriate.

Treatment

• Support

• Psychotherapy

• Drugs

Symptoms may remit spontaneously, particularly when they are mild or of short duration. Mild depression may be treated with general support and psychotherapy. Moderate to severe depression is treated with drugs, psychotherapy, or both and sometimes electroconvulsive therapy. Some patients require a combination of drugs. Improvement may not be apparent until after 1 to 4 wk of drug treatment.

Depression, especially in patients who have had > 1 episode, is likely to recur; therefore, severe cases often warrant long-term maintenance drug therapy.

Most people with depression are treated as outpatients. Patients with significant suicidal ideation, particularly when family support is lacking, require hospitalization, as do those with psychotic symptoms or physical debilitation.

Depressive symptoms in patients with substance abuse disorders often resolve within a few months of stopping substance use. Antidepressant treatment is much less likely to be effective while substance abuse continues.

If a physical disorder or drug toxicity could be the cause, treatment is directed first at the underlying disorder. However, if the diagnosis is in doubt or if symptoms are disabling or include suicidal ideation or hopelessness, a therapeutic trial with an antidepressant or a mood-stabilizing drug may help.

Initial support: Until definite improvement begins, a physician should see patients weekly or biweekly to provide support and education and to monitor progress. Telephone calls may supplement office visits.

Patients and loved ones may be worried or embarrassed about the idea of having a mental disorder. The physician can help by explaining that depression is a serious medical disorder caused by biologic disturbances and requires specific treatment and that the prognosis with treatment is good. Patients and loved ones should be reassured that depression does not reflect a character flaw (eg, laziness, weakness). Telling patients that the path to recovery often fluctuates helps them put feelings of hopelessness in perspective and improves adherence.

Encouraging patients to gradually increase simple activities (eg, taking walks, exercising regularly) and social interactions must be balanced with acknowledging their desire to avoid activities. The physician can suggest that patients avoid self-blame and explain that dark thoughts are part of the disorder and will go away.

Psychotherapy: Psychotherapy, often as cognitive-behavioral therapy (individual or group), alone is often effective for milder forms of depression. Cognitive-behavioral therapy is increasingly used to combat the inertia and self-defeating mental set of depressed patients. However, cognitive-behavioral therapy is most useful when combined with antidepressants to treat moderate to severe depression. Cognitive-behavioral therapy may improve coping skills and enhance gains by providing support and guidance, by removing cognitive distortions that prevent adaptive action, and by encouraging patients to gradually resume social and occupational roles. Couple therapy may help reduce conjugal tensions and disharmony. Long-term psychotherapy is usually unnecessary except for patients who have long-term interpersonal conflicts or who are unresponsive to brief therapy.

Selective serotonin reuptake inhibitors (SSRIs): These drugs prevent reuptake of serotonin (5-hydroxytryptamine [5-HT]). SSRIs include citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, and sertraline. Although these drugs have the same mechanism of action, differences in their clinical properties make selection important. SSRIs have a wide therapeutic margin; they are relatively easy to administer, with little need for dose adjustment (except for fluvoxamine).

By preventing reuptake of 5-HT presynaptically, SSRIs result in more 5-HT to stimulate postsynaptic 5-HT receptors. SSRIs are selective to the 5-HT system but not specific for the different 5-HT receptors. They stimulate 5-HT_1 receptors, with antidepressant and anxiolytic effects, but they also stimulate 5-HT_2 receptors, commonly causing anxiety, insomnia, and sexual dysfunction, and 5-HT_3 receptors, commonly causing nausea and headache. Thus, SSRIs can paradoxically relieve and cause anxiety.

A few patients may seem more agitated, depressed, and anxious within a week of starting SSRIs or increasing the dose. Patients and their loved ones should be warned of this possibility and instructed to call the physician if symptoms worsen with treatment. This situation should be closely monitored because some patients, especially younger children and adolescents, become increasingly suicidal if agitation, increased depression, and anxiety are not detected and rapidly treated. Recent studies have determined that children, adolescents, and young adults have an increased rate of suicidal ideation, suicide gestures, and suicide attempts during the first few months of taking SSRIs (the same concern may apply to serotonin modulators, serotonin-norepinephrine reuptake inhibitors, and norepinephrine-dopamine reuptake inhibitors); physicians must balance this risk with clinical need.

Sexual dysfunction (especially difficulty achieving orgasm but also decreased libido and erectile dysfunction) occurs in one third or more of patients. Some SSRIs cause weight gain. Others, especially fluoxetine, may cause anorexia in the first few months. SSRIs have few anticholinergic, adrenolytic, and cardiac conduction effects. Sedation is minimal or nonexistent, but in the early weeks of treatment, some patients tend to be sleepy during the day. Loose stools or diarrhea occurs in some patients.

Drug interactions are relatively uncommon; however, fluoxetine, paroxetine, and fluvoxamine can inhibit cytochrome P-450 (CYP450) isoenzymes, which can lead to serious drug interactions. For example, these drugs can inhibit the metabolism of certain β-blockers, including propranolol and metoprolol, potentially resulting in hypotension and bradycardia. Discontinuation symptoms (eg, irritability, anxiety, nausea) can occur if the drug is stopped abruptly; such effects are less likely with fluoxetine.

Serotonin modulators (5-HT_2 blockers): These drugs block primarily the 5-HT_2 receptor and inhibit reuptake of 5-HT and norepinephrine. Serotonin modulators include nefazodone, trazodone, and mirtazapine. Serotonin modulators have antidepressant and anxiolytic effects but do not cause sexual dysfunction. Unlike most antidepressants, nefazodone does not suppress REM (rapid eye movement) sleep and produces restful sleep. Nefazodone can significantly interfere with drug-metabolizing liver enzymes and has been associated with liver failure.

Trazodone is related to nefazodone but does not inhibit 5-HT reuptake presynaptically. Unlike nefazodone, trazodone has caused priapism (in 1/1000) and, as an α_1-noradrenergic blocker, may cause orthostatic (postural) hypotension. It is very sedating, so its use in antidepressant doses (> 200 mg/day) is limited. It is most often given in 50- to 100-mg doses at bedtime to depressed patients with insomnia.

Mirtazapine inhibits 5-HT reuptake and blocks α_2-adrenergic autoreceptors, as well as 5-HT_2 and 5-HT_3 receptors. The result is increased serotonergic function and increased noradrenergic function without sexual dysfunction or nausea. It has no cardiac adverse effects, has minimal interaction with drug-metabolizing liver enzymes, and is generally well tolerated, although it does cause sedation and weight gain, mediated by H_1 (histamine) blockade.

Serotonin-norepinephrine reuptake inhibitors: These drugs (eg, venlafaxine, duloxetine) have a dual 5-HT and norepinephrine mechanism of action, as do tricyclic antidepressants. However, their toxicity approximates that of SSRIs. Nausea is the most common problem during the first 2 wk; modest dose-dependent increases in BP occur with high doses. Discontinuation symptoms (eg, irritability, anxiety, nausea) often occur if the drug is stopped suddenly. Duloxetine resembles venlafaxine in effectiveness and adverse effects.

Norepinephrine-dopamine reuptake inhibitors: By mechanisms not clearly understood, these drugs favorably influence catecholaminergic, dopaminergic, and noradrenergic function. They do not affect the 5-HT system.

Bupropion is currently the only drug in this class. It can help depressed patients with concurrent attention-deficit/hyperactivity disorder or cocaine dependence and those trying to stop smoking. Bupropion causes hypertension in a very few patients but has no other effects on the cardiovascular system. Bupropion can cause seizures in 0.4% of patients taking doses > 150 mg tid (or > 200 mg sustained-release [SR] bid or > 450 mg extended-release [XR] once/day); risk is increased in patients with bulimia. Bupropion does not have sexual adverse effects and interacts little with coadministered drugs, although it does inhibit the CYP2D6 hepatic enzyme. Agitation, which is common, is considerably attenuated by using the SR or XR form.

Heterocyclic antidepressants: This group of drugs, once the mainstay of treatment, includes tricyclic (tertiary amines amitriptyline and imipramine and their secondary amine metabolites nortriptyline and desipramine), modified tricyclic, and tetracyclic antidepressants. Acutely, these drugs increase the availability of primarily norepinephrine and, to some extent, 5-HT by blocking reuptake in the synaptic cleft. Long-term use downregulates α_1-adrenergic receptors on the postsynaptic membrane—a possible final common pathway of their antidepressant activity.

Although effective, these drugs are now rarely used because overdose causes toxicity and they have more adverse effects than other antidepressants. The more common adverse effects of heterocyclics are due to their muscarinic-blocking, histamine-blocking, and α_1-adrenolytic actions. Many heterocyclics have strong anticholinergic properties and are thus unsuitable for the elderly and for patients with benign prostatic hypertrophy, glaucoma, or chronic constipation. All heterocyclics, particularly maprotiline and clomipramine, lower the threshold for seizures.

Monoamine oxidase inhibitors (MAOIs): These drugs inhibit the oxidative deamination of the 3 classes of biogenic amines (norepinephrine, dopamine, 5-HT) and other phenylethylamines. MAOIs have little or no effect on normal mood. Their primary value is for treating refractory or atypical depression when SSRIs, tricyclic antidepressants, and sometimes even electroconvulsive therapy is ineffective.

MAOIs marketed as antidepressants in the US (eg, phenelzine, tranylcypromine, isocarboxazid) are irreversible and nonselective (inhibiting MAO-A and MAO-B). Another MAOI (selegiline), which inhibits only MAO-B at lower doses, is available as a patch.

MAOIs that inhibit MAO-A and MAO-B can cause hypertensive crises if a sympathomimetic drug or food containing tyramine or dopamine is ingested concurrently. This effect is called the cheese reaction because mature cheese has a high tyramine content. MAOIs are used infrequently because of concern about this reaction. The lower dosage of the selegiline patch is considered safe to use without specific dietary restrictions, unless the dosage must be higher than starting levels (a 6-mg patch). More selective and reversible MAOIs (eg, moclobemide, befloxatone), which inhibit MAO-A, are not yet available in the US; they are relatively free of these interactions. To prevent hypertension and febrile crises, patients taking MAOIs should avoid sympathomimetic drugs (eg, pseudoephedrine), dextromethorphan, reserpine, and meperidine as well as malted beers, Chianti wines, sherry, liqueurs, and overripe or aged foods that contain tyramine or dopamine (eg, bananas, fava or broad beans, yeast extracts, canned figs, raisins, yogurt, cheese, sour cream, soy sauce, pickled herring, caviar, liver, extensively tenderized meats). Patients can carry 25-mg tablets of chlorpromazine and, as soon as signs of such a hypertensive reaction occur, take 1 or 2 tablets as they head to the nearest emergency department.

Common adverse effects include erectile dysfunction (least common with tranylcypromine), anxiety, nausea, dizziness, insomnia, pedal edema, and weight gain. MAOIs should not be used with other classes of antidepressants, and at least 2 wk (5 wk with fluoxetine, which has a long half-life) should elapse between use of the 2 classes of drugs. MAOIs used with antidepressants that affect the 5-HT system (eg, SSRIs, nefazodone) may cause neuroleptic malignant syndrome (malignant hyperthermia, muscle breakdown, renal failure, seizures, and eventual death). Patients who are taking MAOIs and who also need antiasthmatic or antiallergic drugs, a local anesthetic, or a general anesthetic should be treated by a psychiatrist plus an internist, a dentist, or an anesthesiologist with expertise in neuropsychopharmacology.

Drug choice and administration: Choice of drug may be guided by past response to a specific

antidepressant. Otherwise, SSRIs are often the initial drugs of choice. Although the different SSRIs are equally effective for typical cases, certain properties of the drugs make them more or less appropriate for certain patients (see Table 162-2).

If one SSRI is ineffective, another SSRI can be substituted, but an antidepressant from a different class may be more likely to help. Tranylcypromine in high doses (20 to 30 mg po bid) is often effective for depression refractory to sequential trials of other antidepressants; it should be given by a physician experienced in use of MAOIs. Psychologic

[**Table 162-2.** Antidepressants]

support of patients and loved ones is particularly important in refractory cases.

Insomnia, a common adverse effect of SSRIs, is treated by reducing the dose or adding a low dose of trazodone or another sedating antidepressant. Initial nausea and loose stools usually resolve, but throbbing headaches do not always go away, necessitating a change in drug class. An SSRI should be stopped if it causes agitation. When decreased libido, impotence, or anorgasmia occur during SSRI therapy, dose reduction may help, or a change can be made to another drug class.

SSRIs, which tend to stimulate many depressed patients, should be given in the morning. Giving the entire heterocyclic antidepressant dose at bedtime usually makes sedatives unnecessary, minimizes adverse effects during the day, and improves adherence. MAOIs are usually given in the morning and early afternoon to avoid excessive stimulation.

Therapeutic response with most classes of antidepressants usually occurs in about 2 to 3 wk (sometimes as early as 4 days or as late as 8 wk). For a first episode of mild or moderate depression, the antidepressant should be given for 6 mo, then tapered gradually over 2 mo. If the episode is severe or is a recurrence or if there is suicidal risk, the dose that produces full remission should be continued during maintenance.

For psychotic depression, imipramine appears to be more effective than monotherapy with antidepressants from other classes; dosing this drug can be guided by steady-state plasma levels. The addition of an antipsychotic may improve the likelihood of response, but antipsychotic monotherapy appears to be ineffective.

Continued therapy with an antidepressant for 6 to 12 mo (up to 2 yr in patients > 50) is usually needed to prevent relapse. Most antidepressants, especially SSRIs, should be tapered off (by decreasing the dose by about 25%/wk) rather than stopped abruptly; stopping SSRIs abruptly may result in discontinuation syndrome (nausea, chills, muscles aches, dizziness, anxiety, irritability, insomnia, fatigue). The likelihood and severity of withdrawal varies inversely with the half-life of the SSRI.

Medicinal herbs are used by some patients. St. John's wort (see p. 3431) may be effective for mild depression, although data are contradictory. St. John's wort may interact with other antidepressants and other drugs. A number of placebo-controlled studies of ω-3 supplementation, used as augmentation or as monotherapy, have suggested that eicosapentaenoic acid 1 to 2 g once/day has useful antidepressant effects.

Electroconvulsive therapy (ECT): Severe suicidal depression, depression with agitation or psychomotor retardation, delusional depression, or depression during pregnancy is often treated with ECT if drugs are ineffective. Patients who have stopped eating may need ECT to prevent death. ECT is also effective for psychotic depression. Response to 6 to 10 ECT treatments is usually dramatic and may be lifesaving. Relapse after ECT is common, and drug therapy is often maintained after ECT is stopped.

Phototherapy: Phototherapy is best known for its effects on seasonal depression but can also be effective in other types of depression. Treatment can be provided at home with 2,500 to 10,000 lux at a distance of 30 to 60 cm for 30 to 60 min/day (longer with a less intense light source). In patients who go to sleep late at night and rise late in the morning, phototherapy is most effective in the morning,

sometimes supplemented with 5 to 10 min of exposure between 3 PM and 7 PM. For patients who go to sleep and rise early, phototherapy is most effective between 3 PM and 7 PM.

Other therapies: Psychostimulants (eg, dextroamphetamine, methylphenidate) are sometimes used, often with antidepressants; however, they have not been well studied in controlled clinical trials.

Vagus nerve stimulation involves intermittently stimulating the vagus nerve via an implanted pulse generator. It may be useful for depression refractory to other treatments but usually takes 3 to 6 mo to be effective.

Deep brain stimulation and transcranial magnetic stimulation are still under study.

Bipolar Disorders

Bipolar disorders are characterized by episodes of mania and depression, which may alternate, although many patients have a predominance of one or the other. Exact cause is unknown, but heredity, changes in the level of brain neurotransmitters, and psychosocial factors may be involved. Diagnosis is based on history. Treatment consists of mood-stabilizing drugs, sometimes with psychotherapy.

Bipolar disorders usually begin in the teens, 20s, or 30s. Lifetime prevalence is about 4%. Rates are about equal for men and women.

Bipolar disorders are classified as

- Bipolar I disorder: Defined by the presence of at least one full-fledged (ie, disrupting normal social and occupational function) manic or mixed episode and usually depressive episodes

- Bipolar II disorder: Defined by the presence of major depressive episodes with at least one hypomanic episode but no full-fledged manic episodes

- Bipolar disorder not otherwise specified (NOS): Disorders with clear bipolar features that do not meet the specific criteria for other bipolar disorders

Etiology

Exact cause is unknown. Heredity plays a significant role. There is also evidence of dysregulation of serotonin and norepinephrine. Psychosocial factors may be involved. Stressful life events are often associated with initial development of symptoms and later exacerbations, although cause and effect have not been established. Certain drugs can trigger exacerbations in some patients with bipolar disorder; these drugs include sympathomimetics (eg, cocaine, amphetamines), alcohol, and certain antidepressants (eg, tricyclics, MAOIs).

Symptoms and Signs

Bipolar disorder begins with an acute phase of symptoms, followed by a repeating course of remission and relapse. Remissions are usually complete, although some patients have residual symptoms. Relapses are discrete episodes of more intense symptoms that are manic, depressive, hypomanic, or a mixture of depressive and manic features. Episodes last anywhere from a few weeks to 3 to 6 mo. Cycles —time from onset of one episode to that of the next—vary in length among patients. Some patients have infrequent episodes, perhaps only a few over a lifetime, whereas others have rapid-cycling forms (usually defined as ≥ 4 episodes/yr). Only a minority alternate back and forth between mania and depression with each cycle; in most, one or the other predominates to some extent.

Mania: A manic episode is defined as ≥ 1 wk of a persistently elevated, expansive, or irritable mood plus ≥ 3 additional symptoms:

- Inflated self-esteem or grandiosity

- Decreased need for sleep
- Greater talkativeness than usual
- Persistent elevation of mood
- Flight of ideas or racing of thoughts
- Distractibility
- Increased goal-directed activity

Manic patients are inexhaustibly, excessively, and impulsively involved in various pleasurable, high-risk activities (eg, gambling, dangerous sports, promiscuous sexual activity) without insight into possible harm. Symptoms are so severe that they impair functioning; unwise investments, spending sprees, and other personal choices may have irreparable consequences.

Typically, patients in a manic episode are exuberant and flamboyantly or colorfully dressed; they have an authoritative manner with a rapid, unstoppable flow of speech. Patients may make clang associations (new thoughts that are triggered by word sounds rather than meaning). Easily distracted, patients may constantly shift from one theme or endeavor to another. However, they tend to believe they are in their best mental state. Lack of insight and an increased capacity for activity often lead to intrusive behavior and can be a dangerous combination. Interpersonal friction results and may cause patients to feel that they are being unjustly treated or persecuted. As a result, patients may become a danger to themselves or to other people. Accelerated mental activity is experienced as racing thoughts by patients and is observed as flights of ideas by the physician.

Manic psychosis is a more extreme manifestation, with psychotic symptoms that may be difficult to distinguish from schizophrenia. Patients may have extreme grandiose or persecutory delusions (eg, of being Jesus or being pursued by the FBI), occasionally with hallucinations. Activity level increases markedly; patients may race about and scream, swear, or sing. Mood lability increases, often with increasing irritability. Full-blown delirium (delirious mania) may appear, with complete loss of coherent thinking and behavior.

Hypomania: A hypomanic episode is a less extreme variant of mania involving a distinct episode that lasts ≥ 4 days and is distinctly different from the patient's usual nondepressed mood. During the hypomanic period, mood brightens, the need for sleep decreases, and psychomotor activity accelerates. For some patients, hypomanic periods are adaptive because they produce high energy, creativity, confidence, and supernormal social functioning. Many do not wish to leave the pleasurable, euphoric state. Some function quite well, and in most, functioning is not markedly impaired. However, in some patients, hypomania manifests as distractibility, irritability, and labile mood, which the patient and others find less attractive.

Depression: A depressive episode has features typical of major depression (see p. 1538), including depressed mood, anhedonia, psychomotor retardation, and feelings of pessimism and guilt. Sleeping and eating often increase. Delusions of guilt accompanied by self-loathing are common in psychotic depression, and some patients have hallucinations.

Mixed state: A mixed episode blends depressive and manic or hypomanic features; the criteria for both mania and depression are met. For example, patients may momentarily switch to tearfulness during the height of mania, or their thoughts may race during a depressive period. Often, the switch follows circadian factors (eg, going to bed depressed and waking early in the morning in a hypomanic state). In at least one third of people with bipolar disorder, the entire episode is mixed. A common presentation consists of a dysphorically excited mood, crying, curtailed sleep, racing thoughts, grandiosity, psychomotor restlessness, suicidal ideation, persecutory delusions, auditory hallucinations, indecisiveness, and confusion. This presentation is called dysphoric mania (ie, prominent depressive symptoms superimposed on manic psychosis).

Diagnosis

• Clinical criteria (*Diagnostic and Statistical Manual of Mental Disorders* , Fourth Edition Text Revision)

• Thyroxine (T_4) and thyroid-stimulating hormone (TSH) levels to exclude hyperthyroidism

• Exclusion of stimulant drug abuse clinically or by urine testing

Diagnosis is based on identification of symptoms of mania or hypomania as described above, plus a history of remission and relapse. Some patients who present with depressive symptoms may have previously experienced hypomania or mania but do not report it unless they are specifically questioned. Skillful questioning may reveal morbid signs (eg, excesses in spending, impulsive sexual escapades, stimulant drug abuse), although such information is more likely to be provided by relatives. All patients must be asked gently but directly about suicidal ideation, plans, or activity.

Similar acute manic or hypomanic symptoms may result from stimulant abuse, a schizoaffective disorder (bipolar type), or physical disorders such as hyperthyroidism or pheochromocytoma. A review of substance use (especially of amphetamines and cocaine) and urine drug screening can help identify drug causes. However, because drug use may simply have triggered an episode in a patient with bipolar disorder, seeking evidence of symptoms (manic or depressive) not related to drug use is important. Patients with a schizoaffective disorder rarely return to normal between episodes, and they do not show the interest in connecting with other people manifested by patients with mania (except those with the most florid type). Patients with hyperthyroidism typically have other physical symptoms and signs (see p. 781), but thyroid function testing (T_4 and TSH levels) is a reasonable screen for new patients. Patients with pheochromocytoma are markedly hypertensive; if not, testing is not indicated.

Patients with bipolar disorder may also have anxiety disorders (eg, social phobia, panic attacks, obsessive-compulsive disorders), possibly confusing the diagnosis.

Treatment

• Mood stabilizers (eg, lithium, certain anticonvulsants), a 2nd-generation antipsychotic, or both

• Support and psychotherapy

Treatment usually has 3 phases:

• Acute: To stabilize and control the initial, sometimes severe manifestations

• Continuation: To attain full remission

• Maintenance or prevention: To keep patients in remission

Although most patients with hypomania can be treated as outpatients, severe mania or depression often requires inpatient management.

Drugs for bipolar disorder include mood stabilizers and 2nd-generation antipsychotics. These drugs are used alone or in combination for all phases of treatment, although at different dosages.

Mood stabilizers consist of lithium and certain anticonvulsants, especially valproate, carbamazepine, and lamotrigine. Second-generation antipsychotics include aripiprazole, olanzapine, quetiapine, risperidone, and ziprasidone. Specific antidepressants (eg, SSRIs) are sometimes added for severe depression, but antidepressants (particularly heterocyclics) may trigger mania, and their effectiveness continues to be studied. They are not recommended as sole therapy for depressive episodes.

Electroconvulsive therapy (ECT) is sometimes used for depression refractory to treatment and is also effective for mania. Phototherapy can be useful in treating seasonal bipolar I or bipolar II disorder (with

autumn-winter depression and spring-summer hypomania). It is probably most useful as augmentative therapy.

Drug selection and use: Choice of drug can be difficult because all drugs have significant adverse effects, drug interactions are common, and no drug is universally effective. Selection should be based on what has previously been effective and well tolerated in a given patient. If there is no prior experience (or it is unknown), choice is based on the patient's medical history (vis-a-vis the adverse effects of the specific mood stabilizer) and the severity of symptoms.

For severe manic psychosis, in which immediate patient safety and management is compromised, urgent behavioral control usually requires a sedating 2nd-generation antipsychotic, sometimes supplemented initially with a benzodiazepine such as lorazepam or clonazepam 2 to 4 mg IM or po tid.

For less severe acute episodes in patients without contraindications (eg, renal disorders), lithium is a good first choice for both mania and depressive episodes. Because its onset is slow (4 to 10 days), patients with significant symptoms may also be given an anticonvulsant or a 2nd-generation antipsychotic. For those with depression, lamotrigine may be a good choice of anticonvulsant.

Once remission is achieved, preventive treatment with mood stabilizers is indicated for all bipolar I patients. If episodes recur during maintenance treatment, clinicians should determine whether adherence is poor and, if so, whether nonadherence preceded or followed recurrence. Reasons for nonadherence should be explored to determine whether a change in mood stabilizer type or dosing would render treatment more acceptable.

Lithium: As many as two thirds of patients with uncomplicated bipolar disorder may respond to lithium, which attenuates bipolar mood swings but has no effect on normal mood. Whether lithium or another mood stabilizer is being used, breakthroughs are more likely in patients who have mixed states, rapid-cycling forms of bipolar disorder, comorbid anxiety, substance abuse, or a neurologic disorder.

Lithium carbonate is started at 300 mg po bid or tid and titrated, based on steady-state blood levels and tolerance, to a range of 0.8 to 1.2 mEq/L. Levels should be drawn after 5 days at a stable dose and 12 h after the last dose. Target drug levels for maintenance are lower, about 0.6 to 0.7 mEq/L. Higher maintenance levels are more protective against manic (but not depressive) episodes but have more adverse effects. Adolescents, whose glomerular function is excellent, need higher doses; elderly patients need lower doses.

Lithium can cause sedation and cognitive impairment directly or indirectly (by causing hypothyroidism) and often exacerbates acne and psoriasis. The most common acute, mild adverse effects are fine tremor, fasciculation, nausea, diarrhea, polyuria, polydipsia, and weight gain (partly attributed to drinking high-calorie beverages). These effects are usually transient and often respond to decreasing the dose slightly, dividing the dose (eg, tid), or using slow-release forms. Once dosage is established, the entire dose should be given after the evening meal. This dosing may improve adherence. A β-blocker (eg, atenolol 25 to 50 mg po once/day) can control severe tremor; however, some β-blockers (eg, propranolol) may worsen depression.

Acute lithium toxicity is manifested initially by gross tremor, increased deep tendon reflexes, persistent headache, vomiting, and confusion and may progress to stupor, seizures, and arrhythmias. Toxicity is more likely to occur in elderly patients, in patients with decreased creatinine clearance, and in those with Na loss (eg, due to fever, vomiting, diarrhea, or use of diuretics). Thiazide diuretics, ACE inhibitors, and NSAIDs other than aspirin may contribute to hyperlithemia. Lithium blood levels should be measured every 6 mo and whenever the dose is changed.

Long-term effects include hypothyroidism, particularly when there is a family history of hypothyroidism, and renal damage involving the distal tubule (mainly in patients with a history of renal parenchymal disease). Therefore, TSH levels should be monitored when lithium is started and annually thereafter if there is a family history of thyroid dysfunction or every other year for all other patients. Levels should also be measured whenever symptoms suggest thyroid dysfunction (including when mania recurs) because hypothyroidism may blunt the effect of mood stabilizers. BUN and creatinine should be measured at

baseline, 2 or 3 times during the first 6 mo, and then once or twice a year.

Anticonvulsants: Anticonvulsants that act as mood stabilizers, especially valproate and carbamazepine, are often used for acute mania and for mixed states (mania and depression). Lamotrigine is also effective for mood-cycling and for depression; unlike some antidepressants, it does not induce mania. The precise mechanism of action for anticonvulsants in bipolar disorder is unknown but may involve γ-aminobutyric acid mechanisms and ultimately G-protein signaling systems. Their main advantages over lithium include a wider therapeutic margin and lack of renal toxicity.

For valproate, a loading dose of 20 mg/kg is given, then 250 to 500 mg po tid (extended-release formulation can be used); target blood levels are between 50 and 125 µg/mL. Adverse effects include nausea, headache, sedation, dizziness, and weight gain; rare serious effects include hepatotoxicity and pancreatitis.

Carbamazepine should not be loaded; it should be started at 200 mg po bid and be increased gradually in 200-mg/day increments to target levels between 4 and 12 µg/mL (maximum, 800 mg bid). Adverse effects include nausea, dizziness, sedation, and unsteadiness. Very severe effects include aplastic anemia and agranulocytosis.

Lamotrigine is started at 25 mg po once/day for 2 wk, then 50 mg once/day for 2 wk, then 100 mg/day for 1 wk, and then can be increased by 50 mg each week as needed up to 200 mg once/day. Dosage is lower for patients taking valproate and higher for patients taking carbamazepine. Lamotrigine can cause rash and, rarely, the life-threatening Stevens-Johnson syndrome (see p. 689), particularly if the dosage is increased more rapidly than recommended. While taking lamotrigine, patients should be encouraged to report any new rash, hives, fever, swollen glands, sores in the mouth and on the eyes, and swelling of the lips or tongue.

Antipsychotics: Acute manic psychosis is being increasingly managed with 2nd-generation antipsychotics, such as risperidone (usually 4 to 6 mg po once/day), olanzapine (usually 10 to 20 mg po once/day), quetiapine (200 to 400 mg po bid), ziprasidone (40 to 80 mg po bid), and aripiprazole (10 to 30 mg po once/day). In addition, evidence suggests that these drugs may enhance the effects of mood stabilizers after the acute phase.

Although any of these drugs may have extrapyramidal adverse effects and cause akathisia, risk is lower with more sedating drugs such as quetiapine and olanzapine. Less immediate adverse effects include substantial weight gain and development of the metabolic syndrome (including weight gain, excess abdominal fat, insulin resistance, and dyslipidemia); risk may be lower with the least sedating 2nd-generation antipsychotics, ziprasidone and aripiprazole. For extremely hyperactive psychotic patients with poor food and fluid intake, an antipsychotic given IM plus supportive care in addition to lithium or an anticonvulsant may be appropriate.

Precautions during pregnancy: Lithium use during pregnancy has been associated with an increased risk of cardiovascular malformations (particularly Ebstein's anomaly). However, the absolute risk of this particular malformation is quite low. Taking lithium during pregnancy appears to increase the relative risk of any congenital anomaly by about 2-fold, a risk similar to the 2- to 3-fold increased risk of congenital anomalies associated with use of carbamazepine or lamotrigine and is substantially lower than the risk associated with use of valproate.

Extensive study of the use of 1st-generation antipsychotics and tricyclic antidepressants during early pregnancy has not revealed causes for concern. The same appears to be true of SSRIs, except for paroxetine. Data about the risks of 2nd-generation antipsychotics to the fetus are sparse as yet, even though these drugs are being more widely used for all phases of bipolar disorder.

Use of drugs (particularly lithium and SSRIs) before parturition may have carry-over effects on neonates.

Treatment decisions are complicated by the fact that with unplanned pregnancy, teratogenic effects may already have taken place by the time practitioners' become aware of the issue. Consultation with a perinatal psychiatrist should be considered. In all cases, discussing the risks and benefits of treatment

with patients is important.

Education and psychotherapy: Enlisting the support of loved ones is crucial to preventing major episodes. Group therapy is often recommended for patients and their partner; there, they learn about bipolar disorder, its social sequelae, and the central role of mood stabilizers in treatment. Individual psychotherapy may help patients better cope with problems of daily living and adjust to a new way of identifying themselves.

Patients, particularly those with bipolar II disorder, may not adhere to mood-stabilizer regimens because they believe that these drugs make them less alert and creative. The physician can explain that decreased creativity is relatively uncommon because mood stabilizers usually provide opportunity for a more even performance in interpersonal, scholastic, professional, and artistic pursuits.

Patients should be counseled to avoid stimulant drugs and alcohol, to minimize sleep deprivation, and to recognize early signs of relapse. If patients tend to be financially extravagant, finances should be turned over to a trusted family member. Patients with a tendency to sexual excesses should be given information about conjugal consequences (eg, divorce) and infectious risks of promiscuity, particularly AIDS.

Cyclothymic Disorder

Cyclothymic disorder is characterized by hypomanic and mini-depressive periods that last a few days, follow an irregular course, and are less severe than those in bipolar disorder. Diagnosis is clinical and based on history. Management consists primarily of education, although some patients with functional impairment require drug therapy.

Cyclothymic disorder is commonly a precursor of bipolar II disorder. However, it can also occur as extreme moodiness without becoming a major mood disorder. In chronic hypomania, a form rarely seen clinically, elated periods predominate, with habitual reduction of sleep to < 6 h. People with this form are constantly overcheerful, self-assured, over-energetic, full of plans, improvident, overinvolved, and meddlesome; they rush off with restless impulses and may act in an overfamiliar manner with people.

For some people, cyclothymic and chronic hypomanic dispositions contribute to success in business, leadership, achievement, and artistic creativity; however, they more often have serious detrimental interpersonal and social consequences. Consequences often include instability with an uneven work and schooling history, impulsive and frequent changes of residence, repeated romantic or marital breakups, and an episodic abuse of alcohol and drugs.

Treatment

• Supportive care

• Sometimes a mood stabilizer

Patients should be taught how to live with the extremes of their temperamental inclinations; however, living with cyclothymic disorder is not easy because interpersonal relationships are often stormy. Jobs with flexible hours are advised. Patients with artistic inclinations should be encouraged to pursue careers in the arts because the excesses and fragility of cyclothymia may be better tolerated there.

The decision to use a mood stabilizer depends on the balance between functional impairment and the social benefits or creative spurts that patients may experience. Divalproex 500 to 1000 mg po once/day is often better tolerated than equivalent doses of lithium. Antidepressants should be avoided unless depressive symptoms are severe and prolonged because switching and rapid cycling are risks.

Support groups (eg, Depression and Bipolar Support Alliance in Chicago) can help patients by providing a forum to share their common experiences and feelings.

Chapter 163. Personality Disorders

Introduction

(See also Dissociative Identity Disorder on p. 1505.)

Personality disorders are pervasive, inflexible, and stable patterns of behavior that cause significant distress or functional impairment. Ten distinct personality disorders have been identified and grouped into 3 clusters. All are believed to be caused by a combination of genetic and environmental factors. Diagnosis is clinical. Treatment is with psychotherapy and sometimes drug therapy.

Personality traits are patterns of thinking, perceiving, reacting, and relating that are relatively stable over time and in various situations. Personality traits are usually evident from late adolescence or early adulthood, and although many traits persist throughout much of life, some fade with aging and some can be modified. Personality disorders exist when these traits become so rigid and maladaptive that they impair functioning. Mental coping mechanisms (defenses) that are used unconsciously at times by everyone tend to be immature and maladaptive in people with personality disorders (see Table 163-1).

People with personality disorders are often frustrating and even infuriating to people around them (including physicians). Most are distressed about their lives and have impaired work or social relationships. Personality disorders often coexist with mood, anxiety, substance abuse, and eating disorders. People with severe personality disorders are at high risk of hypochondriasis and violent or self-destructive behaviors. They may have inconsistent, detached, overemotional, abusive, or irresponsible styles of parenting, leading to physical and mental problems in their children.

About 13% of the general population is affected. Antisocial personality disorder occurs in about 2%, with men outnumbering women 6:1. Borderline personality disorder occurs in about 1%, with women outnumbering men 3:1.

Classification

The *Diagnostic and Statistical Manual of Mental Disorders* , Fourth Edition Text Revision (DSM-IV-TR) recognizes 10 distinct personality disorders and divides them into 3 clusters:

A: Odd/eccentric

B: Dramatic/erratic

C: Anxious/fearful

Cluster A: Patients tend to be detached and distrustful.

Paranoid personality involves coldness and distancing in relationships, with a need for control and a tendency toward jealousy if attachments are formed. Affected people are often secretive and untrusting. They tend to be suspicious of changes and frequently find hostile and malevolent motives behind other people's acts. Often, these hostile motives represent projections (see Table 163-1) of their own hostilities onto others. Their reactions

[**Table 163-1.** Coping Mechanisms]

sometimes surprise or scare others. They then use the resulting anger of or rejection by others (ie, projective identification) to justify their original feelings. Paranoid people tend to feel a sense of righteous indignation and often take legal action against others. These people may be highly efficient and conscientious, although they usually need to work in relative isolation. This disorder must be differentiated from paranoid schizophrenia.

Schizoid personality is characterized by introversion, social withdrawal, isolation, and emotional coldness and distancing. Affected people are often absorbed in their own thoughts and feelings and fear closeness and intimacy with other people. They are reticent, are given to daydreaming, and prefer theoretical speculation to practical action.

Schizotypal personality, like schizoid personality, involves social withdrawal and emotional coldness but also includes oddities of thinking, perception, and communication, such as magical thinking, clairvoyance, ideas of reference, or paranoid ideation. These oddities suggest schizophrenia (see p. 1559) but are never severe enough to meet its criteria. People with schizotypal personality are believed to have a muted expression of the genes that cause schizophrenia.

Cluster B: Patients tend to be emotionally unstable, impulsive, and intense.

Borderline personality is marked by unstable self-image, mood, behavior, and relationships. Affected people tend to believe they were deprived of adequate care during childhood and consequently feel empty, angry, and entitled to nurturance. As a result, they relentlessly seek care and are sensitive to its perceived absence. Their relationships tend to be intense and dramatic. When feeling cared for, they appear like lonely waifs who seek help for depression, substance abuse, eating disorders, and past mistreatments. When they fear the loss of the caring person, they frequently express inappropriate and intense anger. These mood shifts are typically accompanied by extreme changes in their view of the world, themselves, and other people—eg, from bad to good, from hated to loved. When they feel abandoned, they dissociate or become desperately impulsive. Their concept of reality is sometimes so poor that they have brief episodes of psychotic thinking, such as paranoid delusions and hallucinations. They often become self-destructive and may cut themselves (self-mutilate) or attempt suicide. They initially tend to evoke intense, nurturing responses in caretakers, but after repeated crises, vague unfounded complaints, and failures to adhere to therapeutic recommendations, they are viewed as help-rejecting complainers. Borderline personality tends to become milder or to stabilize with aging.

Antisocial personality is marked by the callous disregard for the rights and feelings of other people. Affected people exploit others for materialistic gain or personal gratification. They become frustrated easily and tolerate frustration poorly. Characteristically, they act out (see Table 163-1) their conflicts impulsively and irresponsibly, sometimes with hostility and violence. They usually do not anticipate the consequences of their behaviors and typically do not feel remorse or guilt afterward. Many of them have a well-developed capacity for glibly rationalizing their behavior or blaming it on others. Dishonesty and deceit permeate their relationships. Punishment rarely modifies their behavior or improves their judgment. Antisocial personality often leads to alcoholism, drug addiction, promiscuity, failure to fulfill responsibilities, frequent relocation, and difficulty abiding by laws. Life expectancy is decreased, but the disorder tends to diminish or stabilize with age.

Narcissistic personality involves grandiosity. Affected people have an exaggerated sense of superiority and expect to be treated with deference. Their relationships are characterized by a need to be admired, and they are extremely sensitive to criticism, failure, or defeat. When confronted with a failure to fulfill their high opinion of themselves, they can become enraged or seriously depressed and suicidal. They often believe other people envy them. They may exploit others because they think their superiority justifies it.

Histrionic personality involves conspicuous attention seeking. Affected people are also overly conscious of appearance and are dramatic. Their expression of emotions often seems exaggerated, childish, and superficial. Still, they frequently evoke sympathetic or erotic attention from other people. Relationships are often easily established and overly sexualized but tend to be superficial and transient. Behind their seductive behaviors and their tendency to exaggerate somatic problems (ie, hypochondriasis) often lie more basic wishes for dependency and protection.

Cluster C: Patients tend to be nervous and passive or rigid and preoccupied.

Dependent personality is characterized by the surrender of responsibility to other people. Affected people may submit to others to gain and maintain support. For example, they often allow the needs of people they depend on to supersede their own. They lack self-confidence and feel intensely inadequate about taking care of themselves. They believe that others are more capable, and they are reluctant to

express their views for fear that their aggressiveness will offend the people they need. Dependency in other personality disorders may be hidden by obvious behavioral problems; eg, histrionic or borderline behaviors mask underlying dependency.

Avoidant personality is marked by hypersensitivity to rejection and fear of starting relationships or anything new because of the risk of failure or disappointment. Because affected people have a strong conscious desire for affection and acceptance, they are openly distressed by their isolation and inability to relate comfortably to other people. They respond to even small hints of rejection by withdrawing.

Obsessive-compulsive personality is characterized by conscientiousness, orderliness, and reliability, but inflexibility often makes affected people unable to adapt to change. They take responsibilities seriously, but because they hate mistakes and incompleteness, they can become entangled with details and forget their purpose. As a result, they have difficulty making decisions and completing tasks. Such problems make responsibilities a source of anxiety, and they rarely enjoy much satisfaction from their achievements. Most obsessive-compulsive traits are adaptive, and as long as they are not too marked, people who have them often achieve much, especially in the sciences and other academic fields in which order, perfectionism, and perseverance are desirable. However, they can feel uncomfortable with feelings, interpersonal relationships, and situations in which they lack control, they must rely on other people, or events are unpredictable.

Other personality types: Several other personality types have been described but are not classified as disorders in the DSM-IV-TR.

Passive-aggressive (negativistic) personality typically produces the appearance of ineptness or passivity, but these behaviors are covertly designed to avoid responsibility or to control or punish other people. Passive-aggressive behavior is often evidenced by procrastination, inefficiency, or unrealistic protests of disability. Frequently, affected people agree to do tasks they do not want to do and then subtly undermine completion of the tasks. Such behavior usually serves to deny or conceal hostility or disagreements.

Cyclothymic personality (see also p. 1552) alternates between high-spirited buoyancy and gloomy pessimism; each mood lasts weeks or longer. Characteristically, the rhythmic mood changes are regular and occur without justifiable external cause. When these features do not interfere with social adaptation, cyclothymia is considered a temperament and is present in many gifted and creative people.

Depressive personality is characterized by chronic moroseness, worry, and self-consciousness. Affected people have a pessimistic outlook, which impairs their initiative and disheartens other people. Self-satisfaction seems undeserved and sinful. They unconsciously believe their suffering is a badge of merit needed to earn the love or admiration of others.

Diagnosis

• DSM-IV-TR criteria

Specific personality disorders are diagnosed based on DSM-IV-TR criteria. The general criteria in DSM-IV-TR emphasize the need to consider whether other mental or physical disorders (eg, depression, substance abuse, hyperthyroidism) can account for the patient's patterns of behavior.

Patients' emotional reactions and their perspectives on what causes their problems and how other people treat them can provide information about their disorder. Diagnosis is based on observing repetitive patterns of behavior or perceptions that cause distress and impair social functioning. Because the patient often lacks insight into these patterns, physicians may initially seek information from and evaluation by others who interact with the patient. Often, physicians suspect a personality disorder based on their own discomfort, typically if they begin to feel angry or defensive.

Treatment

• Comprehensive approach, often requiring prolonged treatment

Although treatment differs according to the type of personality disorder, some general principles apply:

- Family members and friends can act in ways that either reinforce or diminish the patient's problematic behavior or thoughts; thus, their involvement is helpful and often essential.
- An early effort should be made to get patients to see that the problem is really based on who they are.
- Treating a personality disorder takes a long time; repetitious confrontation in prolonged psychotherapy or by peer encounters is usually required to make patients aware of their defenses, beliefs, and maladaptive behavior patterns.

Because personality disorders are particularly difficult to treat, therapists need experience, enthusiasm, and an understanding of the patient's expected areas of emotional sensitivity and usual ways of coping. Kindness and guidance alone do not change personality disorders. Treatment may involve a combination of psychotherapy and drug therapy. However, symptoms typically are not very responsive to drugs.

Relief of anxiety or depression is the first goal, and drug therapy can be helpful. Reducing environmental stress can also quickly relieve such symptoms.

Maladaptive behaviors, such as recklessness, social isolation, lack of assertiveness, or temper outbursts, can be changed in months. Group therapy and behavior modification, sometimes within day hospital or residential settings, are effective. Participation in self-help groups or family therapy can also help change socially undesirable behaviors. Behavioral change is most important for patients with borderline, antisocial, or avoidant personality disorder. Dialectical behavioral therapy (DBT) is effective for borderline personality disorder. DBT, which involves weekly individual psychotherapy and group therapy as well as telephone contact with therapists between scheduled sessions, seeks to help patients understand their behaviors and teach them problem solving and adaptive behaviors. Psychodynamic therapy is effective for patients with borderline and avoidant personality disorders. Such therapies help patients with personality disorders reorganize feeling states in themselves and think about the effect their behaviors have on other people.

Interpersonal problems, such as dependency, distrust, arrogance, and manipulativeness, usually take > 1 yr to change. The cornerstone for effecting interpersonal changes is individual psychotherapy that helps patients understand the sources of their interpersonal problems. A therapist must repeatedly point out the undesirable consequences of the patient's thought and behavior patterns and must sometimes set limits on the patient's behavior. Such therapy is essential for patients with histrionic, dependent, or passive-aggressive personality disorder. For some patients with personality disorders that involve how attitudes, expectations, and beliefs are mentally organized (eg, narcissistic or obsessive-compulsive types), psychoanalysis is recommended, usually for ≥ 3 yr.

Chapter 164. Schizophrenia and Related Disorders

Introduction

Schizophrenia and related disorders—brief psychotic disorder, delusional disorder, schizoaffective disorder, and schizophreniform disorder—are characterized by psychotic symptoms. Psychotic symptoms include delusions, hallucinations, disorganized thinking and speech, and bizarre and inappropriate behavior.

Brief Psychotic Disorder

Brief psychotic disorder consists of delusions, hallucinations, or other psychotic symptoms for at least 1 day but < 1 mo, with eventual return to normal premorbid functioning. It is typically caused by severe stress in susceptible people.

Brief psychotic disorder is uncommon. Preexisting personality disorders (eg, paranoid, histrionic, narcissistic, schizotypal, borderline) predispose to its development. A major stressor, such as loss of a loved one, may precipitate the disorder. The disorder causes at least one psychotic symptom:

• Delusions

• Hallucinations

• Disorganized speech

• Grossly disorganized or catatonic behavior

This disorder is not diagnosed if a psychotic mood disorder, a schizoaffective disorder, schizophrenia, a physical disorder, or an adverse drug effect (prescribed or illicit) better accounts for the symptoms. Differentiating between brief psychotic disorder and schizophrenia in a patient without any prior psychotic symptoms is based on duration of symptoms; if the duration exceeds 1 mo, the patient no longer meets required diagnostic criteria for brief psychotic disorder.

Treatment is similar to that of an acute exacerbation of schizophrenia; supervision and short-term treatment with antipsychotics may be required.

Delusional Disorder

Delusional disorder is characterized by nonbizarre delusions (false beliefs) that persist for at least 1 mo, without other symptoms of schizophrenia.

Delusional disorder is distinguished from schizophrenia by the presence of delusions without other symptoms of schizophrenia. The delusions tend to be nonbizarre and involve situations that could occur, such as being followed, poisoned, infected, loved at a distance, or deceived by one's spouse or lover.

In contrast to schizophrenia, delusional disorder is relatively uncommon. Onset generally occurs in middle or late adult life. Psychosocial functioning is not as impaired as it is in schizophrenia, and impairments usually arise directly from the delusional belief.

When delusional disorder occurs in elderly patients, it is sometimes called paraphrenia. It may coexist with mild dementia. The physician must be careful to distinguish delusions from elder abuse being reported by a mildly demented elderly patient.

Symptoms and Signs

Delusional disorder may arise from a preexisting paranoid personality disorder (see p. 1553). In such people, a pervasive distrust and suspiciousness of others and their motives begins in early adulthood and extends throughout life. Early symptoms may include the feeling of being exploited, preoccupation with

the loyalty or trustworthiness of friends, a tendency to read threatening meanings into benign remarks or events, persistent bearing of grudges, and a readiness to respond to perceived slights.

Several subtypes of delusional disorder are recognized:

- **Erotomanic:** Patients believe that another person is in love with them. Efforts to contact the object of the delusion through telephone calls, letters, surveillance, or stalking are common. People with this subtype may have conflicts with the law related to this behavior.

- **Grandiose:** Patients believe they have a great talent or have made an important discovery.

- **Jealous:** Patients believe that their spouse or lover is unfaithful. This belief is based on incorrect inferences supported by dubious evidence. They may resort to physical assault.

- **Persecutory:** Patients believe that they are being plotted against, spied on, maligned, or harassed. They may repeatedly attempt to obtain justice through appeals to courts and other government agencies and may resort to violence in retaliation for the imagined persecution.

- **Somatic:** The delusion relates to a bodily function; eg, patients believe they have a physical deformity, odor, or parasite.

Diagnosis

Diagnosis depends largely on making a clinical assessment, obtaining a thorough history, and ruling out other specific conditions associated with delusions. Assessment of dangerousness, especially the extent to which patients are willing to act on their delusion, is very important.

Prognosis

Delusional disorder does not usually lead to severe impairment or change in personality, but delusional concerns may gradually progress. Most patients can remain employed.

Treatment

Treatment aims to establish an effective physician-patient relationship and to manage complications. If patients are assessed to be dangerous, hospitalization may be required. Insufficient data are available to support the use of any particular drug, although antipsychotics sometimes suppress symptoms.

A long-term treatment goal of shifting the patient's major area of concern away from the delusional locus to a more constructive and gratifying area is difficult but reasonable.

Schizoaffective Disorder

Schizoaffective disorder is characterized by significant mood symptoms, psychosis, and other symptoms of schizophrenia. It is differentiated from schizophrenia by occurrence of ≥ 1 episodes of depressive or manic symptoms.

Schizoaffective disorder is considered when a psychotic patient also demonstrates mood symptoms. The diagnosis requires that significant mood symptoms (depressive or manic) be present for a substantial portion of the total duration of illness, concurrent with symptoms of schizophrenia. Differentiating schizoaffective disorder from schizophrenia and mood disorders may require longitudinal assessment of symptoms and symptom progression. The prognosis is somewhat better than that for schizophrenia but worse than that for mood disorders.

Treatment

- Often a combination of drugs, psychotherapy, and community support

Because schizoaffective disorder often leads to long-term disability, comprehensive treatment (including drugs, psychotherapy, and community support) is often required.

For treatment of the manic type, antipsychotics combined with lithium, carbamazepine, or valproate may be more effective than antipsychotics alone.

For treatment of the depressive type, antipsychotics are commonly combined with antidepressants. Antidepressants should usually be introduced once positive psychotic symptoms are stabilized. SSRIs are preferred because of their safety profile. Second-generation antipsychotics may be more effective than conventional antipsychotics in alleviating depression associated with psychosis.

Schizophrenia

Schizophrenia is characterized by psychosis (loss of contact with reality), hallucinations (false perceptions), delusions (false beliefs), disorganized speech and behavior, flattened affect (restricted range of emotions), cognitive deficits (impaired reasoning and problem solving), and occupational and social dysfunction. The cause is unknown, but evidence for a genetic component is strong. Symptoms usually begin in adolescence or early adulthood. One or more episodes of symptoms must last ≥ 6 mo before the diagnosis is made. Treatment consists of drug therapy, psychotherapy, and rehabilitation.

Worldwide, the prevalence of schizophrenia is about 1%. The rate is comparable among men and women and relatively constant cross-culturally. The rate is higher among lower socioeconomic classes in urban areas, perhaps because its disabling effects lead to unemployment and poverty. Similarly, a higher prevalence among single people may reflect the effect of illness or illness precursors on social functioning. The average age at onset is 18 yr in men and 25 yr in women. Onset is rare in childhood, but early-adolescent onset or late-life onset (when it is sometimes called paraphrenia) may occur.

Etiology

Although its specific cause is unknown, schizophrenia has a biologic basis, as evidenced by alterations in brain structure (eg, enlarged cerebral ventricles, decreased size of the anterior hippocampus and other brain regions) and by changes in neurotransmitters, especially altered activity of dopamine and glutamate. Some experts suggest that schizophrenia occurs in people with neurodevelopmental vulnerabilities and that the onset, remission, and recurrence of symptoms are the result of interactions between these enduring vulnerabilities and environmental stressors.

Neurodevelopmental vulnerability: Vulnerability may result from genetic predisposition; intrauterine, birth, or postnatal complications; or viral CNS infections. Maternal exposure to famine and influenza during the 2nd trimester of pregnancy, birth weight < 2500 g, Rh incompatibility during a 2nd pregnancy, and hypoxia increase risk.

Although most people with schizophrenia do not have a family history, genetic factors have been implicated. People who have a 1st-degree relative with schizophrenia have about a 10% risk of developing the disorder, compared with a 1% risk among the general population. Monozygotic twins have a concordance of about 50%. Sensitive neurologic and neuropsychiatric tests suggest that aberrant smooth-pursuit eye tracking, impaired cognition and attention, and deficient sensory gating occur more commonly among patients with schizophrenia than among the general population. These markers (endophenotypes) also occur among 1st-degree relatives of people with schizophrenia and may represent the inherited component of vulnerability.

Environmental stressors: Stressors can trigger the emergence or recurrence of symptoms in vulnerable people. Stressors may be primarily biochemical (eg, substance abuse, especially marijuana) or social (eg, becoming unemployed or impoverished, leaving home for college, breaking off a romantic relationship, joining the Armed Forces); however, these stressors are not causative. There is no evidence that schizophrenia is caused by poor parenting.

Protective factors that may mitigate the effect of stress on symptom formation or exacerbation include

good social support, coping skills, and antipsychotics (see Treatment on p. 1562).

Symptoms and Signs

Schizophrenia is a chronic illness that may progress through several phases, although duration and patterns of phases can vary. Patients with schizophrenia tend to develop psychotic symptoms an average of 12 to 24 mo before presenting for medical care.

Phases: In the premorbid phase, patients may show no symptoms or may have impaired social competence, mild cognitive disorganization or perceptual distortion, a diminished capacity to experience pleasure (anhedonia), and other general coping deficiencies. Such traits may be mild and recognized only in retrospect or may be more noticeable, with impairment of social, academic, and vocational functioning.

In the prodromal phase, subclinical symptoms may emerge; they include withdrawal or isolation, irritability, suspiciousness, unusual thoughts, perceptual distortions, and disorganization. Onset of overt schizophrenia (delusions and hallucinations) may be sudden (over days or weeks) or slow and insidious (over years).

In the middle phase, symptomatic periods may be episodic (with identifiable exacerbations and remissions) or continuous; functional deficits tend to worsen.

In the late illness phase, the illness pattern may be established, and disability may stabilize or even diminish.

Symptom categories: Generally, symptoms are categorized as

• Positive: An excess or distortion of normal functions

• Negative: Diminution or loss of normal functions

• Disorganized: Thought disorders and bizarre behavior

• Cognitive: Deficits in information processing and problem solving

Patients may have symptoms from one or all categories.

Positive symptoms can be further categorized as delusions and hallucinations. Delusions are erroneous beliefs. In persecutory delusions, patients believe they are being tormented, followed, tricked, or spied on. In delusions of reference, patients believe that passages from books, newspapers, song lyrics, or other environmental cues are directed at them. In delusions of thought withdrawal or thought insertion, patients believe that others can read their mind, that their thoughts are being transmitted to others, or that thoughts and impulses are being imposed on them by outside forces. Hallucinations may be auditory, visual, olfactory, gustatory, or tactile, but auditory hallucinations are by far the most common. Patients may hear voices commenting on their behavior, conversing with one another, or making critical and abusive comments. Delusions and hallucinations may be extremely vexing to patients.

Negative (deficit) symptoms include blunted affect, poverty of speech, anhedonia, and asociality. With blunted affect, the patient's face appears immobile, with poor eye contact and lack of expressiveness. Poverty of speech refers to decreased speech and terse replies to questions, creating the impression of inner emptiness. Anhedonia may be reflected by a lack of interest in activities and increased purposeless activity. Asociality is shown by a lack of interest in relationships. Negative symptoms often lead to poor motivation and a diminished sense of purpose and goals.

Disorganized symptoms, which can be considered a type of positive symptom, involve thought disorders and bizarre behaviors. Thinking is disorganized, with rambling, non-goal-directed speech that shifts from one topic to another. Speech can range from mildly disorganized to incoherent and incomprehensible. Bizarre behavior may include childlike silliness, agitation, and inappropriate appearance, hygiene, or conduct. Catatonia is an extreme behavior that can include maintaining a rigid

posture and resisting efforts to be moved or engaging in purposeless and unstimulated motor activity.

Cognitive deficits include impairment in attention, processing speed, working memory, abstract thinking, problem solving, and understanding of social interactions. The patient's thinking may be inflexible, and the ability to problem solve, understand the viewpoints of other people, and learn from experience may be diminished. Symptoms of schizophrenia typically impair the ability to function and often markedly interfere with work, social relations, and self-care. Unemployment, isolation, deteriorated relationships, and diminished quality of life are common outcomes. Severity of cognitive impairment is a major determinant of overall disability.

Subtypes: Five subtypes of schizophrenia have been described:

- Paranoid: Characterized by delusions or auditory hallucinations, with preservation of cognition and affect

- Disorganized: Characterized by disorganized speech, disorganized behavior, and flat or inappropriate affect

- Catatonic: Characterized by physical symptoms, including either immobility or excessive motor activity and the assumption of bizarre postures

- Residual: A clear history of schizophrenia with more prominent symptoms, followed by a prolonged period of mild negative symptoms

- Undifferentiated: A mixture of symptoms from the other subtypes

Alternatively, some experts classify schizophrenia into deficit and nondeficit subtypes based on the presence and severity of negative symptoms, such as blunted affect, lack of motivation, and diminished sense of purpose. Patients with the deficit subtype have prominent negative symptoms unaccounted for by other factors (eg, depression, anxiety, an understimulating environment, drug adverse effects). Those with the nondeficit subtype may have delusions, hallucinations, and thought disorders but are relatively free of negative symptoms.

Suicide: About 10% of patients with schizophrenia commit suicide. Suicide is the major cause of premature death among people with schizophrenia and explains, in part, why on average the disorder reduces life span by 10 yr. Patients who have paranoid subtypes with late onset and good premorbid functioning—the very patients with the best prognosis for recovery—are also at the greatest risk of suicide. Because these patients retain the capacity for grief and anguish, they may be more prone to act in despair based on a realistic recognition of the effect of their disorder (see also p. 1579).

Violence: Schizophrenia is a relatively modest risk factor for violent behavior. Threats of violence and minor aggressive outbursts are far more common than seriously dangerous behavior. Patients more likely to engage in significant violence include those with substance abuse, persecutory delusions, or command hallucinations and those who do not take their prescribed drugs. A very few severely depressed, isolated, paranoid patients attack or murder someone whom they perceive as the single source of their difficulties (eg, an authority, a celebrity, their spouse).

Diagnosis

- Combination of history, symptoms, and signs

No definitive test for schizophrenia exists. Diagnosis is based on a comprehensive assessment of history, symptoms, and signs. Information from collateral sources, such as family members, friends, teachers, and coworkers, is often important. According to the *Diagnostic and Statistical Manual of Mental Disorders* , Fourth Edition Text Revision (DSM-IV-TR), the diagnosis requires both of the following:

- ≥ 2 characteristic symptoms (delusions, hallucinations, disorganized speech, disorganized behavior, negative symptoms) for a significant portion of a 1-mo period

- Prodromal or attenuated signs of illness with social, occupational, or self-care impairments evident for a 6-mo period that includes 1 mo of active symptoms

Psychosis due to other medical disorders or substance abuse must be ruled out by history and examination that includes laboratory tests and neuroimaging (see p. 1487). Although some patients with schizophrenia have structural brain abnormalities present on imaging, these abnormalities are insufficiently specific to have diagnostic value.

Other mental disorders with similar symptoms include several that are related to schizophrenia: brief psychotic disorder, schizophreniform disorder, schizoaffective disorder, and delusional disorder. In addition, mood disorders can cause psychosis in some people. Certain personality disorders (especially schizotypal) cause symptoms similar to those of schizophrenia, although they are usually milder and do not involve psychosis.

Prognosis

During the first 5 yr after onset of symptoms, functioning may deteriorate and social and work skills may decline, with progressive neglect of self-care. Negative symptoms may increase in severity, and cognitive functioning may decline. Thereafter, the level of disability tends to plateau. Some evidence suggests that severity of illness may lessen in later life, particularly among women. Spontaneous movement disorders may develop in patients who have severe negative symptoms and cognitive dysfunction, even when antipsychotics are not used.

Prognosis varies depending on the subtype. Patients with paranoid schizophrenia tend to be less severely disabled and more responsive to available treatments. Patients with the deficit subtype are typically more disabled, have a poorer prognosis, and are more resistant to treatment.

Schizophrenia can occur with other mental disorders. When associated with significant obsessive-compulsive symptoms (see p. 1495), prognosis is particularly poor; with symptoms of borderline personality disorder (see p. 1555), prognosis is better. About 80% of people with schizophrenia experience one or more episodes of major depression at some time in their life.

For the first year after diagnosis, prognosis is closely related to adherence to prescribed psychoactive drugs. Overall, one third of patients achieve significant and lasting improvement; one third improve somewhat but have intermittent relapses and residual disability; and one third are severely and permanently incapacitated. Only about 15% of all patients fully return to their pre-illness level of functioning.

Factors associated with a good prognosis include

- Good premorbid functioning (eg, good student, strong work history)
- Late and/or sudden onset of illness
- Family history of mood disorders other than schizophrenia
- Minimal cognitive impairment
- Few negative symptoms
- Paranoid or nondeficit subtype

Factors associated with a poor prognosis include

- Young age at onset
- Poor premorbid functioning

• Family history of schizophrenia

• Disorganized or deficit subtype with many negative symptoms

Men have poorer outcomes than women; women respond better to treatment with antipsychotics.

Substance abuse is a significant problem in up to 50% of patients with schizophrenia. Anecdotal evidence suggests that use of marijuana and other hallucinogens is highly disruptive for patients with schizophrenia and should be strongly discouraged. Comorbid substance abuse is a significant predictor of poor outcome and may lead to drug nonadherence, repeated relapse, frequent rehospitalization, declining function, and loss of social support, including homelessness.

Treatment

• Antipsychotic drugs

• Rehabilitation, including community support services

• Psychotherapy

The time between onset of psychotic symptoms and first treatment correlates with the rapidity of initial treatment response, quality of treatment response, and severity of negative symptoms. When treated early, patients tend to respond more quickly and fully. Without ongoing use of antipsychotics after an initial episode, 70 to 80% of patients have a subsequent episode within 12 mo. Continuous use of antipsychotics can reduce the 1-yr relapse rate to about 30%.

General goals are to reduce severity of psychotic symptoms, prevent recurrences of symptomatic episodes and associated deterioration of functioning, and help patients function at the highest level possible. Antipsychotics, rehabilitation with community support services, and psychotherapy are the major components of treatment. Because schizophrenia is a long-term and recurrent illness, teaching patients illness self-management skills is a significant overall goal.

Drugs are divided into conventional antipsychotics and 2nd-generation antipsychotics (SGAs) based on their specific neurotransmitter receptor affinity and activity. SGAs may offer some advantages both in terms of modestly greater efficacy (although recent evidence casts doubt on SGAs' advantage as a class) and reduced likelihood of an involuntary movement disorder and related adverse effects. However, risk of metabolic syndrome (excess abdominal fat, insulin resistance, dyslipidemia, and hypertension) is greater with SGAs than with conventional antipsychotics.

Conventional antipsychotics: These drugs (see Table 164-1) act primarily by blocking the dopamine-2 receptor (dopamine-2 blockers). Conventional antipsychotics can be classified as high, intermediate, or low potency. High-potency antipsychotics have a higher affinity for dopamine receptors and less for α-adrenergic and muscarinic receptors. Low-potency antipsychotics, which are rarely used, have less affinity for dopamine receptors and relatively more affinity for α-adrenergic, muscarinic, and histaminic receptors. Different drugs are available in tablet, liquid, and short- and long-acting IM preparations. A specific drug is selected primarily based on adverse effect profile, required route of administration, and the patient's previous response to the drug.

Two conventional antipsychotics (and one SGA) are available as long-acting depot preparations (see Table 164-2). These preparations are useful for eliminating drug nonadherence. They may also help patients who, because of disorganization, indifference, or denial of illness, cannot reliably take daily oral drugs.

Conventional antipsychotics have several adverse effects, such as sedation, cognitive blunting, dystonia and muscle stiffness, tremors, elevated prolactin levels, and weight gain (for treatment of adverse effects, see Table 157-4 on p. 1493). Akathisia (motor restlessness) is particularly unpleasant and may lead to

nonadherence. These drugs may also cause tardive dyskinesia, an involuntary movement disorder most often characterized by puckering of the lips and tongue, writhing of the arms or legs, or both. The incidence of tardive dyskinesia is about 5%/yr of drug exposure among patients taking conventional antipsychotics. In about 2%, tardive dyskinesia is severely disfiguring. In some patients, tardive dyskinesia persists indefinitely, even after the drug is stopped. Because of this risk, patients receiving long-term maintenance therapy should be evaluated at least every 6 mo. Rating instruments, such as the Abnormal Involuntary Movement Scale, may be used (see Table 164-3). Neuroleptic malignant syndrome, a rare but potentially fatal adverse

[**Table 164-1.** Conventional Antipsychotics]

[**Table 164-2.** Depot Antipsychotic Drugs]

effect, is characterized by rigidity, fever, autonomic instability, and elevated CK.

About 30% of patients with schizophrenia do not respond to conventional antipsychotics. They may respond to clozapine, an SGA.

Second-generation antipsychotics: SGAs block dopamine receptors more selectively than conventional antipsychotics, decreasing the likelihood of extrapyramidal (motor) adverse effects. Although greater binding to serotonergic receptors was initially thought to contribute to the efficacy of SGAs, recent studies suggest this binding is unrelated to efficacy or adverse effect profile. SGAs also do the following:

- Tend to alleviate positive symptoms
- May lessen negative symptoms to a greater extent than do conventional antipsychotics (although such differences have been questioned)
- May cause less cognitive blunting
- Are less likely to have extrapyramidal (motor) adverse effects
- Have a lower risk of causing tardive dyskinesia
- Increase prolactin slightly or not at all (except risperidone, which increases prolactin as much as do conventional antipsychotics)

Clozapine, the first SGA, is the only SGA shown to be effective in up to 50% of patients resistant to conventional antipsychotics. Clozapine reduces negative symptoms, has few or no motor adverse effects, and has minimal risk of causing tardive dyskinesia, but it has other adverse effects, including sedation, hypotension, tachycardia, weight gain, type 2 diabetes, and increased salivation. It also may cause seizures in a dose-dependent fashion. The most serious adverse effect is agranulocytosis, which can occur in about 1% of patients. Consequently, frequent monitoring of WBCs is required, and clozapine is generally reserved for patients who have responded inadequately to other drugs.

Newer SGAs (see Table 164-4) provide some of the benefits of clozapine without the risk of agranulocytosis and are generally preferable to conventional antipsychotics for treatment of an acute episode and for prevention of recurrence. However, in a recent, large, long-term, controlled clinical trial, symptom relief using any of 4 SGAs (olanzapine, risperidone, quetiapine, ziprasidone) was no greater than that with perphenazine, a conventional antipsychotic. A follow-up study, in which patients who left the study prematurely were randomized to one of the 3 other study SGAs or to clozapine, demonstrated a clear advantage of clozapine over the other SGAs. Hence, clozapine seems to be the only effective treatment for patients who have failed treatment with a conventional antipsychotic or an SGA. However, clozapine remains underused, probably because of lower tolerability and need for continuous blood monitoring.

Newer SGAs are very similar to each other in efficacy but differ in adverse effects, so drug choice is based on individual response and on other drug characteristics. For example, olanzapine, which has a

relatively high rate of sedation, may be prescribed for patients with prominent agitation or insomnia; less sedating drugs might be preferred for patients with lethargy. A 4- to 8-wk trial is usually required to assess efficacy. After acute symptoms have stabilized, maintenance treatment is initiated; for it, the lowest dose that prevents symptom recurrence is used. Risperidone is the only SGA available in a long-acting injectable formulation.

Weight gain, hyperlipidemia, and elevated risk of type 2 diabetes are the major adverse effects of SGAs. Thus, before treatment with SGAs is begun, all patients should be screened for risk factors, including personal or family history of diabetes, weight, waist circumference, BP, and fasting plasma glucose and lipid profile. Those found to have or to be at significant risk of metabolic syndrome may be better treated with ziprasidone or aripiprazole than

[Table 164-3. Abnormal Involuntary Movement Scale]

the other SGAs. Patient and family education regarding symptoms and signs of diabetes, including polyuria, polydipsia, weight loss, and diabetic ketoacidosis (nausea, vomiting, dehydration, rapid respiration, clouding of sensorium), should be provided. In addition, nutritional and physical activity counseling should be provided to all patients when they start taking an SGA. All patients taking an SGA require periodic monitoring of weight, body mass index, and fasting plasma glucose and referral for specialty evaluation if they develop hyperlipidemia or type 2 diabetes.

Rehabilitation and community support services: Psychosocial skill training and vocational rehabilitation programs help many patients work, shop, and care for themselves; manage a household; get along with others; and work with mental health care practitioners. Supported employment, in which patients are placed in a competitive work setting and provided with an on-site job coach to promote adaptation to work, may be particularly valuable. In time, the job coach acts only as a backup for problem solving or for communication with employers.

Support services enable many patients with schizophrenia to reside in the community. Although most can live independently, some require supervised apartments where a staff member is present to ensure drug adherence. Programs provide a graded level of supervision in different residential settings, ranging from 24-h support to periodic home visits. These programs help promote patient autonomy while providing sufficient care to minimize the likelihood of relapse and need for inpatient hospitalization. Assertive community treatment programs provide services in the patient's home or other residence and are based on high staff-to-patient ratios; treatment teams directly provide all or nearly all required treatment services.

Hospitalization or crisis care in a hospital alternative may be required during severe relapses, and involuntary hospitalization may

[Table 164-4. Second-Generation Antipsychotics*]

be necessary if patients pose a danger to themselves or others. Despite the best rehabilitation and community support services, a small percentage of patients, particularly those with severe cognitive deficits and those poorly responsive to drug therapy, require long-term institutional or other supportive care.

Psychotherapy: The goal of psychotherapy is to develop a collaborative relationship between the patients, family members, and physician so that patients can learn to understand and manage their illness, take drugs as prescribed, and handle stress more effectively. Although individual psychotherapy plus drug therapy is a common approach, few empirical guidelines are available. Psychotherapy that begins by addressing the patient's basic social service needs, provides support and education regarding the nature of the illness, promotes adaptive activities, and is based on empathy and a sound dynamic understanding of schizophrenia is likely to be most effective. Many patients need empathic psychologic support to adapt to what is often a lifelong illness that can substantially limit functioning.

For patients who live with their families, psychoeducational family interventions can reduce the rate of relapse. Support and advocacy groups, such as the National Alliance for the Mentally Ill, are often helpful

to families.

Schizophreniform Disorder

Schizophreniform disorder is characterized by symptoms identical to those of schizophrenia but that last ≥ 1 mo but < 6 mo.

At presentation, schizophrenia is likely to be suspected. Psychosis secondary to substance abuse or to a physical disorder must also be ruled out. Differentiating between schizophreniform disorder and schizophrenia in a patient without any prior psychotic symptoms is based on duration of symptoms. If duration of symptoms or disability exceeds 6 mo, the patient no longer meets required diagnostic criteria for schizophreniform disorder, and the diagnosis is likely to be schizophrenia, although the acute psychosis may also evolve into a psychotic mood disorder, such as bipolar or schizoaffective disorder. Longitudinal observation is often required to establish the diagnosis and appropriate treatment.

Treatment with antipsychotics and supportive psychosocial care is indicated. After symptoms resolve, drug treatment is continued for 12 mo and then gradually tapered while closely monitoring for the return of psychotic symptoms.

Substance-Induced Psychotic Disorder

Psychotic symptoms, particularly delusions and hallucinations, can result from a wide variety of substances, including alcohol, amphetamines, marijuana, cocaine, hallucinogens, inhalants, opioids, phencyclidine, and certain sedatives and anxiolytics.

Diagnosis

The diagnosis is made when symptoms begin during or < 1 mo after intoxication with or withdrawal from the implicated substance and after other psychotic disorders are ruled out. Because symptoms may overlap with brief psychotic disorder, schizophreniform disorder, and acute episodes of psychotic mania or schizophrenia, differentiating these conditions may be difficult. Diagnosis may require several days of observation.

Treatment

• Symptomatic

Treatment may vary depending on the drug involved. Hallucinogen and phencyclidine psychosis may not respond well to antipsychotics. A supportive approach is preferred, with reassuring, structured, and protective surroundings. Agitation may be best treated with short-acting benzodiazepines, such as lorazepam given po or IM.

Chapter 165. Sexuality and Sexual Disorders

Introduction

(For sexual dysfunction in men, see p. 2345; for sexual dysfunction in women, see p. 2521.)

Accepted norms of sexual behavior and attitudes vary greatly within and among different cultures. Health care practitioners should never be judgmental of sexual behaviors, even under societal pressure. Generally, what is normal and abnormal cannot be defined medically. However, when sexual behavior or difficulties bother a patient or the patient's partner or cause harm, treatment is warranted.

Societal attitudes about sexuality also change with time, as has occurred with the following:

- **Masturbation:** Once widely regarded as a perversion and a cause of mental disorders, masturbation is now recognized as a normal sexual activity throughout life. It is considered abnormal only when it inhibits partner-oriented behavior, is done in public, or is sufficiently compulsive to cause distress. About 97% of males and 80% of females masturbate. Although masturbation is harmless, guilt created by the disapproval and punitive attitudes of other people may cause considerable distress and impair sexual performance. Masturbation often continues at some level even in a sexually healthy relationship.

- **Homosexuality:** Homosexuality has not been considered a disorder by the American Psychiatric Association for > 3 decades. About 4 to 5% of the population identify themselves as exclusively homosexual for their entire lives. Like heterosexuality, homosexuality results from complex biologic and environmental factors leading to an ability to become sexually aroused by people of the same sex. Like heterosexuality, homosexuality is not a matter of choice.

- **Promiscuity:** Frequent sexual activity with many partners, often involving anonymous or one-time-only encounters, may indicate a diminished capacity for intimacy. However, promiscuity is not in itself evidence of a psychosexual disorder. Casual sex is common, although the fear of AIDS, herpes simplex infections, and other sexually transmitted diseases has resulted in a decrease.

- **Extramarital sex:** Most cultures discourage extramarital sexual activity but accept premarital or nonmarital sexual activity as normal. In the US, most people engage in sexual activity before marriage or without marriage as part of the trend toward more sexual freedom in developed countries. Extramarital sex occurs frequently among married people despite social taboos. This behavior has the potential to pass diseases to unsuspecting spouses.

Accepted norms of sexual behavior and attitudes are influenced greatly by parents. A forbidding, puritanical rejection of physical affection, including touching, by a parent engenders guilt and shame in children and inhibits their capacity for enjoying sex and developing healthy intimate relationships as adults. Relations with parents may be damaged by excessive emotional distance, by punitive behaviors, or by overt seductiveness and sexual exploitation. Children exposed to verbal and physical hostility, rejection, and cruelty are likely to develop problems with sexual and emotional intimacy. For example, love and sexual arousal may become dissociated, so that although emotional bonds can be formed with people from the same social class or intellectual circle, sexual relationships can be formed only with those for whom there is no emotional intimacy, typically those who are perceived to be of a lower class or in some way depreciated (eg, prostitutes, anonymous partners).

Well-informed health care practitioners can offer sensitive, disciplined advice on sexuality and should not miss opportunities for helpful intervention. Behaviors that place patients at risk of sexually transmitted diseases must be addressed. Practitioners have an opportunity to recognize and address psychosexual issues, including sexual dysfunction (see pp. 2345 and 2521), gender identity problems, and paraphilias.

Gender Identity Disorder and Transsexualism

Gender identity disorder is characterized by a strong, persistent cross-gender identification; people believe they are victims of a biologic accident and are cruelly imprisoned in a body incompatible with their subjective gender identity. Those with the most extreme form of gender

identity disorder are called transsexuals. These disorders are considered mental disorders because the body does not match the person's psychologic (felt) gender.

Core gender identity is a subjective sense of knowing to which gender one belongs, ie, the awareness that "I am a male" or "I am a female." Gender *identity* is the inner sense of masculinity or femininity. Gender *role* is the objective, public expression of being male, female, or androgynous (blended). It is everything that people say and do to indicate to others or to themselves the degree to which they are male or female. For most people, there is congruity between their anatomic sex, gender identity, and gender role. However, those with gender identity disorder experience some degree of incongruity between their anatomic sex and their gender identity. The incongruity experienced by transsexuals is usually complete, severe, disturbing, and long-standing. Labeling the condition a "disorder" can add to the distress that frequently occurs, and the term should not be construed as being judgmental. Treatment is aimed at helping patients adapt rather than trying to dissuade them from their identity; in any case, the latter approach is ineffective.

Gender role behaviors fall on a continuum of traditional masculinity or femininity, with a growing cultural recognition that some people do not fit into the traditional male-female dichotomy. Western cultures are more tolerant of tomboyish behaviors in young girls (generally not considered a gender identity disorder) than effeminate or "sissy" behaviors in boys. Many boys role-play as girls or mothers, including trying on their sister's or mother's clothes. Usually, this behavior is part of normal development. Only in extreme cases does this behavior and an associated expressed wish to be the other sex persist. Most boys with gender identity disorder of childhood do not have the disorder as adults, but many are homosexual or bisexual as adults.

Etiology

Although biologic factors (eg, genetic complement, prenatal hormonal milieu) largely determine gender identity, the formation of a secure, unconflicted gender identity and gender role is influenced by social factors (eg, the character of the parents' emotional bond, the relationship that each parent has with the child). Rarely, transsexualism is associated with genital ambiguity or a genetic abnormality (eg, Turner's syndrome, Klinefelter's syndrome).

When sex labeling and rearing are confusing (eg, in cases of ambiguous genitals or genetic syndromes altering genital appearance, such as androgen insensitivity syndrome), children may become uncertain about their gender identity or role, although the level of importance of environmental factors remains controversial. However, when sex labeling and rearing are unambiguous, even the presence of ambiguous genitals often does not affect a child's gender identity.

Symptoms and Signs

Childhood gender identity problems are usually present by age 2. Children experiencing difficulty with gender identity commonly do the following:

• Prefer cross-dressing

• Insist that they are of the other sex

• Intensely and persistently desire to participate in the stereotypical games and activities of the other sex

• Have negative feelings toward their genitals

For example, a young girl may insist she will grow a penis and become a boy; she may stand to urinate. A boy may fantasize about being female, and avoid rough-and-tumble play and competitive games. He may sit to urinate and wish to be rid of his penis and testes. For boys with a gender identity disorder, distress at the physical changes of puberty is often followed by a request during adolescence for feminizing somatic treatments. Most children with these disorders are not evaluated until they are age 6 to 9, at a point when the disorder is already chronic.

Although most transsexuals began having gender identity problems in early childhood, some do not present until adulthood. Male-to-female transsexuals may be cross-dressers first and only later in life come to accept their cross-gender identity. Marriage and military service are common among transsexual men who seek to run from their cross-gender feelings. Once they accept their cross-gender (transgender) feelings, many transsexuals adopt a convincing public feminine gender role. Some are satisfied with mastering a more feminine appearance and obtaining an identity card (eg, driver's license) as a female to help them work and live in society as women. Others experience problems, which may include depression and suicidal behavior.

Diagnosis

Diagnosis in children requires the presence of both of the following:

• Cross-gender identification (the desire to be or insistence that they are the other sex)

• A sense of discomfort about their sex or sense of substantial inappropriateness in their gender role

Cross-gender identification must not be merely a desire for perceived cultural advantages of being the other sex. For example, a boy who says he wants to be a girl so that he will receive the same special treatment his younger sister receives is not likely to have gender identity disorder.

Assessment of adults focuses on determining whether there is significant distress or obvious impairment in social, occupational, or other important areas of functioning.

Treatment

• For selected, motivated patients, hormone therapy, sex reassignment surgery, and psychotherapy

Cross-gender behavior, such as cross-dressing, may not require treatment if it occurs without concurrent psychologic distress or functional impairment or if a person has a physical intersex condition (eg, congenital adrenal hyperplasia, ambiguous genitals, androgen insensitivity syndrome).

Most transsexuals who request treatment are natal males who claim a feminine gender identity and regard their genitals and masculine features with repugnance. However, as treatments improve, female-to-male transsexualism is increasingly seen in medical and psychiatric practice. Transsexuals' primary objective in seeking medical help is not to obtain psychologic treatment but to obtain hormones and genital surgery that will make their physical appearance approximate their felt gender identity. The combination of psychotherapy, hormonal reassignment, and sex reassignment surgery is often curative when the disorder is appropriately diagnosed and clinicians follow the internationally accepted standards of care for the treatment of gender identity disorders, available from the World Professional Association for Transgender Health (WPATH).

Male-to-female transsexualism: Taking moderate doses of a feminizing hormone (eg, ethinyl estradiol 0.1 mg once/day) plus electrolysis and other feminizing treatments may make the adjustment to a feminine gender role more stable.

Many male-to-female transsexuals request sex reassignment surgery. Surgery involves removal of the penis and testes and creation of an artificial vagina. A part of the glans penis is retained as a clitoris, which is usually sexually sensitive and retains the capacity for orgasm in most cases. The decision to pursue sex reassignment surgery often raises important social problems for patients. Many of these patients are married and have children. A parent or spouse who changes sex will have substantial adjustment issues in all intimate relationships and may lose loved ones in the process. In follow-up studies, genital surgery has helped some transsexuals live happier and more productive lives and so is justified in highly motivated, appropriately assessed and treated transsexuals who have completed a 1- to 2-yr real-life experience in the opposite gender role. Before surgery, transsexuals often need assistance with passing in public, including help with gestures and voice modulation. Participation in gender support groups, available in most large cities, is usually helpful.

Female-to-male transsexualism: Patients ask for mastectomy early, then hysterectomy and oophorectomy. Androgenic hormones (eg, IM testosterone ester preparations 300 to 400 mg q 3 wk or equivalent doses of androgen transdermal patches or gels) are given to permanently alter the voice, induce a more masculine muscle and fat distribution, and promote growth of facial and body hair.

Patients may opt for an artificial phallus (neophallus) to be fashioned from skin transplanted from the inner forearm (phalloplasty) or for a micropenis to be created from fat tissue removed from the testosterone-hypertrophied clitoris (metoidioplasty). Surgery may help certain patients achieve greater adaptation and life satisfaction. Similar to male-to-female transsexuals, female-to-male transsexuals should live in the male gender role for at least 1 yr before surgery. Anatomic results of neophallus surgical procedures are often less satisfactory in terms of function and appearance than neovaginal procedures for male-to-female transsexuals. Complications are common, especially in procedures that involve extending the urethra into the neophallus.

Paraphilias

Paraphilias are recurrent, intense, sexually arousing fantasies, urges, or behaviors that are distressing or disabling and that involve inanimate objects, children or other nonconsenting adults, or suffering or humiliation of oneself or the partner.

Sexual preferences that seem unusual to another person or health care practitioner do not constitute paraphilia simply because they are unusual. The arousal patterns are considered pathologic only when the following apply:

- They become obligatory for sexual functioning (ie, erection or orgasm cannot occur without the stimulus).
- They involve inappropriate partners (eg, children, nonconsenting adults).
- They cause significant distress or impairment in social, occupational, or other important areas of functioning.

People with a paraphilia may have an impaired or nonexistent capacity for affectionate, reciprocal emotional and sexual intimacy with a consenting partner. Other aspects of personal and emotional adjustment may be impaired as well.

The pattern of disturbed erotic arousal is usually fairly well developed before puberty. At least 3 processes are involved:

- Anxiety or early emotional trauma interferes with normal psychosexual development.
- The standard pattern of arousal is replaced by another pattern, sometimes through early exposure to highly charged sexual experiences that reinforce the person's experience of sexual pleasure.
- The pattern of sexual arousal often acquires symbolic and conditioning elements (eg, a fetish symbolizes the object of arousal but may have been chosen because the fetish was accidentally associated with sexual curiosity, desire, and excitement).

Whether all paraphilic development results from these psychodynamic processes is controversial, and some evidence of altered brain functioning is present in some paraphilias (eg, pedophilia).

In most cultures, paraphilias are far more common among males. Biologic reasons for the unequal distribution may exist but are poorly defined.

Many of the paraphilias are rare. The most common are pedophilia, voyeurism, transvestic fetishism, and exhibitionism. Some paraphilias (such as pedophilia) are illegal and may result in being imprisoned and being labeled and registered as a sex offender for life. Some of these offenders have significant personality disorders accompanying the paraphilia (eg, antisocial, narcissistic), which make treatment

difficult. Often, more than one paraphilia is present.

Fetishism

Fetishism is use of an inanimate object (the fetish) as the preferred method of producing sexual excitement. However, in common parlance, the word is often used to describe particular sexual interests, such as sexual role-playing, preference for certain physical characteristics, and preferred sexual activities.

Common fetishes include aprons, shoes, leather or latex items, and women's underclothing. The fetish may replace typical sexual activity with a partner or may be integrated into sexual activity with a willing partner. Minor fetishistic behavior as an adjunct to consensual sexual behavior is not considered a disorder because distress, disability, and significant dysfunction are absent. More intense, obligatory fetishistic arousal patterns may cause problems in a relationship or become all-consuming and destructive in a person's life.

Transvestic fetishism: Heterosexual males who dress in women's clothing typically begin such behavior in late childhood (see also Gender Identity Disorder and Transsexualism on p. 1568). A more common term for transvestite is cross-dresser. This behavior is associated, at least initially, with sexual arousal.

Cross-dressing per se is not a disorder because this behavior does not always cause distress or impairment. Personality profiles of cross-dressing men are generally similar to age- and race-matched norms. When their partner is cooperative, these men have intercourse in partial or full feminine attire. When their partner is not cooperative, they may feel anxiety, depression, guilt, and shame associated with the desire to cross-dress.

Most transvestites do not present for treatment. Those who do are usually brought in by an unhappy spouse, referred by courts, or self-referred out of concern about experiencing negative social and employment consequences. Some transvestites present for treatment of comorbid gender dysphoria, substance abuse, or depression. Social and support groups for transvestites are usually very helpful. No drugs are reliably effective; psychotherapy is aimed at self-acceptance and modulating risky behaviors.

Exhibitionism

Exhibitionism is characterized by achievement of sexual excitement through genital exposure, usually to an unsuspecting stranger. It may also refer to a strong desire to be observed by other people during sexual activity.

Exhibitionists (usually male) may masturbate while exposing or fantasizing about exposing themselves. They may be aware of their need to surprise, shock, or impress the unwilling observer. The victim is almost always a female adult or a child of either sex. Actual sexual contact is rarely sought. Age at onset is usually the mid 20s; occasionally, the first act occurs during preadolescence or middle age. About 30% of apprehended male sex offenders are exhibitionists. They have the highest recidivism rate of all sex offenders; about 20 to 50% are re-arrested. Most exhibitionists are married, but the marriage is often troubled by poor social and sexual adjustment, including frequent sexual dysfunction. Very few females are diagnosed as exhibitionists; society sanctions some exhibitionistic behaviors in females (through media and entertainment venues).

For some people, exhibitionism is expressed as a strong desire to have other people watch their sexual acts. What appeals to such people is not the act of surprising an audience but rather of being seen by a consenting audience. People with this form of exhibitionism may make pornographic films or become adult entertainers. They are rarely troubled by this desire and thus may not have a psychiatric disorder.

Treatment

When laws are broken and sex offender status is conferred, treatment usually begins with psychotherapy, support groups, and SSRIs (see p. 1573). If these drugs are ineffective, antiandrogens should be considered; full informed consent and appropriate monitoring of liver function and serum testosterone

levels are required.

Voyeurism

Voyeurism is achievement of sexual arousal by observing people who are naked, disrobing, or engaging in sexual activity. When observation is of unsuspecting people, this sexual behavior often leads to problems with the law and relationships.

Desire to watch others in sexual situations is common and not in itself abnormal. Voyeurism usually begins during adolescence or early adulthood. Adolescent voyeurism is generally viewed more leniently; few teenagers are arrested. When voyeurism is pathologic, voyeurs spend considerable time seeking out viewing opportunities. Orgasm is usually achieved by masturbating during or after the voyeuristic activity. Voyeurs do not seek sexual contact with the people being observed.

In many cultures, voyeurs have ample legal opportunities to watch sexual activity.

Treatment

When laws are broken and sex offender status is conferred, treatment usually begins with therapy, support groups, and SSRIs (see p. 1573). If these drugs are ineffective, antiandrogens should be considered; full informed consent and appropriate monitoring of liver function and serum testosterone levels are required.

Sexual Masochism

Sexual masochism is intentional participation in an activity that involves being humiliated, beaten, bound, or otherwise abused to experience sexual excitement.

Sadomasochistic fantasies and sexual behavior between consenting adults is very common. Masochistic activity tends to be ritualized and chronic. For most participants, the humiliation and beating are simply acted out; participants know that it is a game and carefully avoid actual humiliation or injury. However, some masochists increase the severity of their activity with time, potentially leading to serious injury or death.

Masochistic activities may be the preferred or exclusive mode of producing sexual excitement. People may act on their masochistic fantasies themselves (eg, binding themselves, piercing their skin, applying electrical shocks, burning themselves) or seek out a partner who may be a sexual sadist. Activities with a partner include bondage, blindfolding, spanking, flagellation, humiliation by means of urination or defecation on the person, forced cross-dressing, or simulated rape.

Treatment of this disorder is often ineffective.

Sexual Sadism

Sexual sadism is infliction of physical or mental suffering (eg, humiliation, terror) on the sex partner to stimulate sexual excitement and orgasm.

Most sexual sadists have insistent, persistent fantasies in which sexual excitement results from suffering inflicted on the partner, consenting or not. Mild sadism is a common sexual practice; when it becomes pathologic is a matter of degree. Sexual sadism is not rape, a complex amalgam of sex and power over the victim. Sexual sadism is diagnosed in < 10% of rapists.

Most sadistic sexual behavior occurs between consenting adults. As is the case with masochism, sadism is usually limited in scope and not harmful. In some people, the behaviors escalate to the point of harm. When practiced with nonconsenting partners, sexual sadism constitutes criminal activity and is likely to continue until the sadist is apprehended. Sexual sadism is particularly dangerous when associated with antisocial personality disorder (see p. 1555). This combination of disorders is particularly recalcitrant to any form of psychiatric treatment.

Pedophilia

(See also p. 3063.)

Pedophilia is a preference for sexual activity with prepubertal children. Pedophilia often leads to imprisonment; medical management should include drugs and psychotherapy.

Sexual offenses against children constitute a significant proportion of reported criminal sexual acts. Arbitrarily, the age of a person with pedophilia is set at ≥ 16 yr, with the age difference between offender and child victim set at ≥ 5 yr. The age of the child is usually ≤ 13 yr. For older adolescents with pedophilia (ie, 17 to 18 yr old), no precise age difference is specified; clinical and legal judgment is relied on. Legal criteria may be different from psychiatric criteria.

Most pedophiles are male. Attraction may be to young boys, girls, or both. But pedophiles prefer opposite-sex to same-sex children 2:1. In most cases, the adult is known to the child and may be a family member, stepparent, or a person with authority (eg, a teacher). Looking or touching seems more prevalent than genital contact. Homosexual males typically have a less close acquaintanceship with the child. Pedophiles may be attracted only to children (exclusive) or also adults (nonexclusive).

Some pedophiles limit their sexual activities to their own children or to close relatives (incest). Predatory pedophiles, many of whom have antisocial personality disorder, may use force and threaten to physically harm the child or the child's pets if the abuse is disclosed. The course of pedophilia is chronic, and perpetrators often have or develop substance abuse or dependence and depression. Pervasive family dysfunction, including marital conflict, is common.

Identifying a pedophile often poses an ethical crisis for health care practitioners. They can try to protect the privacy of the patient but must protect the community of children. Practitioners should know the reporting requirements in their state. If practitioners have reasonable suspicion of child sexual or physical abuse, it must be reported to authorities.

Treatment

• Psychotherapy

• Treatment of associated disorders

• Drug treatment (eg, antiandrogens, SSRIs)

Long-term individual or group psychotherapy is usually necessary and may be especially helpful when it is part of multimodal treatment that includes social skills training, treatment of comorbid physical and mental disorders (eg, seizure disorders, attention deficit disorder, depression), and drug treatment. Treatment is less effective when court ordered, although many adjudicated sex offenders have benefited from treatments, such as group psychotherapy and antiandrogens.

In the US, IM medroxyprogesterone acetate is the treatment of choice; cyproterone is used in Europe. Typical doses are medroxyprogesterone 200 mg IM 2 to 3 times/wk for 2 wk, followed by 200 mg 1 to 2 times/wk for 4 wk, then 200 mg q 2 to 4 wk. Serum testosterone should be monitored and maintained in the normal female range (< 62 ng/dL). Treatment is usually long-term because deviant fantasies usually recur weeks to months after treatment is stopped. Drugs that inhibit gonadotropin release (eg, leuprolide, goserelin), given IM, have also been used. Liver function tests and serum testosterone levels should be monitored as required.

The usefulness of antiandrogens in female pedophiles is less well established.

In addition to antiandrogens, SSRIs (eg, high-dose fluoxetine 60 to 80 mg po once/day or fluvoxamine 200 to 300 mg po once/day) may be useful. Drugs are most effective when used as part of a multimodal treatment program.

Some pedophiles who are committed to treatment and monitoring can refrain from pedophilic activity and be reintegrated into society.

Chapter 166. Somatoform and Factitious Disorders

Introduction

Somatization is the expression of mental phenomena as physical (somatic) symptoms. Typically, the symptoms cannot be explained by a physical disorder. Disorders characterized by somatization extend in a continuum from those in which symptoms develop unconsciously and nonvolitionally to those in which symptoms develop consciously and volitionally. This continuum includes somatoform disorders, factitious disorders, and malingering. Somatization typically leads to seeking medical evaluation and treatment.

Somatoform disorders are characterized by physical symptoms that are not fully explained by another disorder—physical or mental. Symptoms of somatoform disorders are not volitional. Somatoform disorders are distressing and often impair social, occupational, academic, or other aspects of functioning. These disorders include body dysmorphic disorder, conversion disorder, hypochondriasis, pain disorder, somatization disorder, undifferentiated somatoform disorder, and somatoform disorder not otherwise specified. Body dysmorphic disorder differs somewhat from other somatoform disorders in that it is characterized by preoccupation with perceived defects in physical appearance.

Factitious disorders involve the conscious and volitional feigning of symptoms without any external incentive (eg, time off from work) and is thus distinguished from malingering. Patients gain gratification from assuming the sick role through the simulation, exaggeration, or aggravation of symptoms and signs. Symptoms and signs may be mental, physical, or both. The most severe and chronic form is Munchausen syndrome.

Malingering is intentional feigning of physical or mental symptoms motivated by an external incentive (eg, feigning illness to avoid work or military duty, to evade criminal prosecution, or to obtain financial compensation or drugs for abuse). Malingering is suspected in the following cases:

- Patients report symptoms, yet little is detected through unannounced observation, physical examination, or laboratory testing.
- The claimed disability and objective findings are markedly discrepant.
- Patients do not cooperate with efforts to diagnose or treat potential causes of symptoms.

Body Dysmorphic Disorder

Body dysmorphic disorder is preoccupation with an imagined or a slight defect in appearance that causes significant distress or impairment of social, occupational, academic, or other aspects of functioning. Diagnosis is based on history. Treatment consists of drug therapy, psychotherapy, or both.

Body dysmorphic disorder usually begins during adolescence and may be somewhat more common among women.

Symptoms and Signs

Symptoms may develop gradually or abruptly. Although intensity may vary, the disorder is usually chronic unless patients are appropriately treated. Concerns commonly involve the face or head but may involve any body part or several parts and may change from one part to another. For example, patients may be concerned about thinning hair, acne, wrinkles, scars, vascular markings, color of complexion, or excessive facial or body hair. Or they may focus on the shape or size of the nose, eyes, ears, mouth, breasts, buttocks, legs, or other body part. Men may have a form of the disorder called muscle dysmorphia, which involves preoccupation with the idea that their body is not sufficiently lean and muscular.

Patients usually spend many hours a day worrying about their perceived defects. Most check themselves often in mirrors, others avoid mirrors, and still others alternate between the 2 behaviors. Other common

compulsive behaviors include excessive grooming, skin picking, reassurance seeking, and clothes changing. Most try to camouflage their imagined defects—eg, by growing a beard to hide perceived scars or by wearing a hat to cover slightly thinning hair. Many undergo cosmetic, medical (most often, dermatologic), dental, or surgical treatment to correct their perceived defect, but such treatment is usually unsuccessful and may intensify their preoccupation. Men with muscle dysmorphia may use androgen supplements.

Because people with body dysmorphic disorder feel self-conscious about their appearance, they may avoid going out in public. For most, social, occupational, academic, and other aspects of functioning are impaired because of their concerns about appearance. Some leave their homes only at night; others, not at all. Social isolation, repeated hospitalization, and suicidal behavior may result.

Diagnosis

• History

Because many patients are too embarrassed and ashamed to reveal their symptoms, the disorder may go undiagnosed for years. It is distinguished from normal concerns about appearance because the preoccupations are time-consuming and cause significant distress, impairment in functioning, or both.

Diagnosis is based on history. If the only concern is body shape and weight, an eating disorder may be the more accurate diagnosis (see p. 1535); if the only concern is the appearance of sex characteristics, gender identity disorder may be considered (see p. 1568).

Treatment

Serotonin reuptake inhibitors are often effective and are currently the drug of choice; relatively high doses are often required. Cognitive-behavioral therapy that specifically targets symptoms of body dysmorphic disorder is currently the psychotherapy of choice.

Conversion Disorder

Conversion disorder consists of symptoms or deficits that develop unconsciously and nonvolitionally and usually involve motor or sensory function. Manifestations resemble a neurologic or other physical disorder but rarely conform to known pathophysiologic mechanisms or anatomic pathways. Onset, exacerbation, or maintenance of conversion symptoms is typically attributed to mental factors, such as stress. Diagnosis is based on history after excluding physical disorders as the cause. Treatment begins by establishing a consistent, supportive physician-patient relationship; psychotherapy can help, as may hypnosis.

Conversion disorder tends to develop during late childhood to early adulthood but may occur at any age. It is more common among women.

Symptoms and Signs

Symptoms often develop abruptly, and onset can often be linked to a stressful event. Symptoms involve apparent deficits in voluntary motor or sensory function and sometimes include seizures, thus suggesting a neurologic or general physical disorder. For example, patients may present with impaired coordination or balance, weakness, paralysis of an arm or a leg, loss of sensation in a body part, seizures, blindness, double vision, deafness, aphonia, difficulty swallowing, sensation of a lump in the throat, or urinary retention.

The symptoms are severe enough to cause significant distress or impair social, occupational, or other important areas of functioning. Patients may have a single episode or sporadic repeated ones; symptoms may become chronic. Typically, episodes are brief.

Diagnosis

The diagnosis is considered only after a physical examination and tests rule out physical disorders that can fully account for the symptoms and their effects.

Treatment

A consistently trustful and supportive physician-patient relationship is essential. Collaborative treatment that involves a psychiatrist and a physician from another field (eg, neurologist, internist) seems most helpful. After the physician has excluded a physical disorder and reassured patients that the symptoms do not indicate a serious underlying disorder, patients may begin to feel better, and symptoms may fade.

The following treatments may help:

- Hypnosis may help by enabling patients to control the effects of stress and their mental state on their bodily functions.

- Narcoanalysis is a rarely used procedure similar to hypnosis except that patients are given a sedative to induce a state of semisleep.

- Psychotherapy, including cognitive-behavioral therapy, is effective for some people.

Any coexisting psychiatric disorders (eg, depression) should be treated.

Hypochondriasis

Hypochondriasis is preoccupation with the fear of having, or with the idea that one has, a serious disease, based on misinterpretation of nonpathologic physical symptoms or normal bodily functions. Hypochondriasis is nonvolitional; the exact cause is unknown. Diagnosis is confirmed when fears and symptoms persist for ≥ 6 mo despite reassurance after thorough medical evaluation. Treatment includes establishing a consistent, supportive physician-patient relationship; cognitive-behavioral therapy and drug therapy may help.

Hypochondriasis most commonly begins during early adulthood and appears to occur equally among men and women.

Symptoms and Signs

A wide array of fears may derive from misinterpreting nonpathologic physical symptoms or normal bodily functions (eg, borborygmi, abdominal bloating and crampy discomfort, heartbeat, sweating). The location, quality, and duration of symptoms are often described in minute detail, but symptoms are usually not associated with abnormal physical findings. Symptoms impair social and occupational functioning or cause significant distress.

The course is often chronic—fluctuating in some, steady in others. Some patients recover.

Diagnosis

The diagnosis is suggested by the history and confirmed when symptoms persist ≥ 6 mo despite appropriate medical evaluation that excludes a physical disorder and reassurance, and when the symptoms are not better accounted for by depression or another mental disorder.

Treatment

Treatment is difficult because patients believe that something is seriously wrong and that the physician has failed to find the real cause. A trusting relationship with a caring, reassuring physician can nonetheless prove beneficial. If symptoms are not adequately relieved, patients may benefit from a psychiatric referral while continuing under the care of the primary physician.

Treatment with SSRIs may be helpful, as may cognitive-behavioral therapy.

Munchausen Syndrome

Munchausen syndrome, a severe and chronic form of factitious disorder, consists of intentional production or feigning of physical symptoms or signs without an external incentive; the motivation for this behavior is to assume the sick role. Symptoms are usually acute, dramatic, and convincing and are accompanied by a tendency to wander from one physician or hospital to another for treatment. The exact cause is unknown, although stress and a severe personality disorder, most often borderline personality disorder, are often implicated.

Patients with Munchausen syndrome may simulate many physical symptoms or conditions (eg, MI, hematemesis, hemoptysis, diarrhea, FUO). Their abdominal wall may be crisscrossed by scars, or a digit or a limb may have been amputated. Fevers are often due to self-inflicted injection with bacteria; *Escherichia coli* is often the infecting organism. These patients initially and sometimes chronically become the responsibility of medical or surgical clinics. Nevertheless, the disorder is a mental problem, is more complex than simple dishonest simulation of symptoms, and is associated with severe emotional difficulties.

Patients may have prominent histrionic or borderline personality features and are usually intelligent and resourceful. They know how to simulate disease and are sophisticated regarding medical practices. They differ from malingerers because although their deceits and simulations are conscious and volitional, their behavior is not motivated by external incentives, such as economic gain. It is unclear what they gain beyond medical attention for their suffering, and their motivations and quest for attention are largely unconscious and obscure.

Patients may have an early history of emotional and physical abuse. Patients may also have experienced a severe illness during childhood or had a seriously ill relative. Patients appear to have problems with their identity as well as unstable relationships. Feigning illness may be a way to increase or protect self-esteem by blaming failures on their illness, by being associated with prestigious physicians and medical centers, and by appearing unique, heroic, or medically knowledgeable and sophisticated.

Diagnosis

Diagnosis is based on history and examination, along with any tests necessary to exclude physical disorders. Less severe forms of factitious disorder may also involve the feigning of physical or mental symptoms (eg, depression, hallucinations, delusions, symptoms of posttraumatic stress disorder), with an apparent goal to assume the sick role. These forms are not considered Munchausen, which is more severe and chronic, with recurrent hospitalization, peregrination, and pseudologia fantastica (lying in a manner that is intriguing to the listener).

Treatment

• No clearly effective treatments

Treatment is usually challenging, and there are no clearly effective treatments. Patients may obtain initial relief by having their treatment demands met, but their symptoms typically escalate, ultimately surpassing what physicians are willing or able to do. Confrontation or refusal to meet treatment demands often results in angry reactions, and patients usually move from one physician or hospital to another (called peregrination). Recognizing the disorder and requesting psychiatric or psychologic consultation early is important, so that risky invasive testing, surgical procedures, and excessive or unwarranted use of drugs can be avoided.

A nonaggressive, nonpunitive, nonconfrontational approach should be used to present the diagnosis of Munchausen syndrome or other forms of factitious disorder to patients. To avoid suggesting guilt or reproach, a physician can present the diagnosis as a cry for help. Alternatively, some experts recommend providing mental health treatment without requiring patients to admit their role in causing their illness. In either case, conveying that the physician and patient can cooperatively resolve the problem is helpful.

Munchausen Syndrome by Proxy

Munchausen syndrome by proxy is a variant in which caregivers (usually a parent) intentionally produce or feign physical or mental symptoms or signs in a person in their care (usually a child).

The caregiver falsifies history and may injure the child with drugs or other agents or add blood or bacterial contaminants to urine specimens to simulate disease. The caregiver seeks medical care for the child and appears to be deeply concerned and protective. The child typically has a history of frequent hospitalizations, usually for a variety of nonspecific symptoms, but no firm diagnosis. Victimized children may be seriously ill and sometimes die.

Pain Disorder

(Somatoform Pain Disorder)

Pain disorder consists of pain in one or more anatomic sites severe enough to warrant clinical attention and to cause clinically significant distress or impairment of social, occupational, or other functioning. Mental factors are judged to have an important role in the onset, severity, exacerbation, or maintenance of symptoms, but the pain is not intentionally produced or feigned. Some patients may recall an initial stimulus that produced acute pain. Diagnosis is based on history. Treatment begins by establishing a consistent, supportive physician-patient relationship; drug therapy and psychotherapy can also help.

The proportion of people whose chronic pain is strongly influenced by mental factors is unknown. However, pain is rarely, if ever, "all in a patient's head"; apperception of pain involves sensory and emotional components (see p. 1620). In some cases, both mental and physical factors have important roles in the onset, severity, exacerbation, or maintenance of the pain.

Symptoms and Signs

Physical pain may occur in mood and anxiety disorders, but in pain disorder, pain is a major complaint and is severe enough to warrant clinical attention. Any body part may be affected; the back, head, abdomen, and chest are commonly involved. The pain may be acute or chronic (≥ 6 mo).

Diagnosis

Diagnosis is based on history after excluding a physical disorder that would adequately explain the pain and its onset, severity, duration, and maintenance and the degree of disability. Detection of mental or social stressors may help explain the disorder.

Treatment

- Effective treatment of pain
- For chronic pain, measures that correct dysfunction caused by pain's effects (eg, psychotherapy, various drugs)

A thorough medical evaluation, followed by reassurance, may be sufficient. Sometimes, empathetically pointing out a relationship with an obvious mental or social stressor is effective. However, many patients develop chronic problems and are difficult to treat. They may visit many physicians with an expressed wish to find a cure and are at risk of developing dependence on opioids or benzodiazepines.

For acute pain, the primary goal is to relieve the pain with analgesics, most commonly NSAIDs and acetaminophen. Antidepressants and anticonvulsants are sometimes added.

For chronic pain (lasting ≥ 6 mo), it is important to not only manage the pain but also to reduce the pain's effect on the patient's life and functioning. Psychotherapy and various drugs (eg, analgesics, antidepressants, anticonvulsants) may help. Opioids can be safely and effectively used for chronic pain,

although some patients abuse and become dependent on them, especially those with a history of substance abuse and dependence. All patients need ongoing monitoring for abuse and dependence. Thorough regular reevaluations by a caring, empathetic physician, who remains alert to the possibility of a new significant physical disorder while protecting the patient from unnecessary tests or procedures, offers hope for long-term palliation.

Somatization Disorder

Somatization disorder is characterized by multiple physical complaints (eg, pain; GI, sexual, and neurologic symptoms) over several years that cannot be explained fully by a physical disorder. Symptoms usually begin before age 30 and are not intentionally produced or feigned. Diagnosis is based on history after excluding physical disorders. Treatment focuses on establishing a consistent, supportive physician-patient relationship that avoids exposing the patient to unnecessary diagnostic testing and therapies.

Somatization disorder is often familial, although the etiology is unknown. Somatization disorder occurs more often in women. Male relatives of affected women have an increased risk of antisocial personality and substance-related disorders.

Symptoms and Signs

Recurring and multiple physical complaints usually begin before age 30. Severity may fluctuate, but symptoms persist for at least several years. Complete symptom relief for any extended period is rare. Some people become more overtly depressed.

Any body part may be affected, and specific symptoms and their frequency vary among cultures. In the US, typical symptoms include headache, nausea and vomiting, bloating, abdominal pain, diarrhea or constipation, dysuria, dysmenorrhea, dyspareunia, and loss of sexual desire. Men frequently complain of erectile or ejaculatory dysfunction. Neurologic symptoms are also present. Anxiety and depression may occur. Typically, patients are dramatic and emotional when recounting their symptoms, often referring to them as "unbearable," "beyond description," or "the worst imaginable."

Patients may become dependent on others, demanding help and emotional support and becoming angry when they feel their needs are not met. They may also threaten or attempt suicide. Often dissatisfied with their medical care, they typically go from one physician to another or seek treatment from several physicians concurrently.

The intensity and persistence of symptoms may reflect a strong desire to be cared for. Symptoms may help patients avoid responsibilities but may also prevent pleasure and act as punishment, suggesting underlying feelings of unworthiness and guilt.

Diagnosis

• Usually clinical criteria

Patients are unaware of their underlying mental problem and believe that they have physical ailments, so they pressure physicians for tests and treatments. Physicians usually do many examinations and tests to eliminate a physical disorder as the cause. Because such patients may develop concurrent physical disorders, appropriate examinations and tests should also be done when symptoms change significantly or when objective signs develop. Patients, even those who have a satisfactory relationship with a primary physician, are commonly referred to a psychiatrist.

Specific diagnostic criteria include the following:

• Onset of multiple physical symptoms before age 30

• Symptoms occurring over several years

- Treatment seeking or impaired functioning
- Pain affecting ≥ 4 body parts
- ≥ 2 GI symptoms other than pain (eg, nausea, bloating, food intolerance)
- ≥ 1 sexual or reproductive symptom other than pain (eg, sexual indifference, erectile dysfunction)
- ≥ 1 neurologic symptom other than pain (eg, weakness, imbalance, loss of sensation)

The diagnosis is supported by the dramatic nature of the complaints and the patient's sometimes exhibitionistic, dependent, and suicidal behavior. Somatization disorder is distinguished from generalized anxiety disorder, conversion disorder, and major depression by the predominance, multiplicity, and persistence of physical symptoms.

Patients who do not meet the above diagnostic criteria for somatization disorder but who have ≥ 6 mo of ≥ 1 physical complaints that are not fully explained by a physical disorder or another mental disorder and who have clinically significant distress or impairment in functioning, are said to have undifferentiated somatoform disorder.

Treatment

Treatment is usually difficult. Drug treatment of concurrent mental disorders (eg, depression) may help. Psychotherapy, particularly cognitive-behavioral therapy, may also help. Patients benefit from having a supportive relationship with a primary care physician, who coordinates all of their health care, offers symptomatic relief, sees them regularly, and protects them from unnecessary tests and procedures.

Chapter 167. Suicidal Behavior

Introduction

Suicidal behavior includes 3 types of self-destructive acts: completed suicide, attempted suicide, and suicide gestures. Thoughts and plans about suicide are referred to as suicide ideation.

Completed suicide is a suicidal act that results in death. Attempted suicide is an act intended to be self-lethal, but one that does not result in death. Frequently, suicide attempts involve at least some ambivalence about wishing to die and may be a cry for help. Suicide gestures are attempts that involve an action with a very low lethal potential (eg, inflicting superficial scratches on the wrist, overdosing on vitamins). Suicide gestures and suicide ideation may reflect pleas for help from people who still wish to live. However, they should not be dismissed lightly.

Epidemiology

Statistics on suicidal behavior are based mainly on death certificates and inquest reports and underestimate the true incidence. Suicide ranks 11th among causes of death in the US, with 32,439 completed suicides in 2004. It is the 3rd leading cause of death among people 10 to 24 yr. Men ≥ 75 have the highest rate of death by suicide. In all age groups, male deaths by suicide outnumber female deaths by 4:1.

Each year, an estimated > 700,000 people attempt suicide. About 25 attempts are made for every death that occurs by suicide. However, 3.5 to 12.5% of people who make an attempt eventually die by suicide because many people make repeated attempts. About 20 to 30% of people who attempt suicide try again within 1 yr. Women attempt suicide twice as often as men, but men complete suicide 4 times more often than women.

People in a secure relationship have a significantly lower suicide rate than single people. Attempted and completed suicide rates are higher among those who live alone. Suicide is less common among practicing members of most religious groups (particularly Roman Catholics).

Group suicides, whether of many people or only 2 (such as lovers or spouses), represent an extreme form of personal identification with others.

A suicide note is left by about 1 in 6 people who complete suicide. The content may indicate the mental disorder that led to the suicidal act.

Etiology

Suicidal behaviors usually result from the interaction of several factors. The primary remediable risk factor in suicide is

• Depression

Suicide and suicide attempts appear to be more common among patients with anxiety disorders, and severe anxiety is associated with major depression or bipolar disorders.

Other factors include the following:

• Social factors

• Personality abnormalities

• Traumatic childhood experiences

• Serious physical disorders

• Alcohol and drugs of abuse

• Serious psychiatric disorders

Certain social factors (eg, disappointment, loss) and personality abnormalities (eg, impulsivity, aggression) appear associated with suicide. Traumatic childhood experiences, particularly the distresses of a broken home, parental deprivation, and abuse, are significantly more common among people who commit suicidal acts. Suicide is sometimes the final act in a course of self-destructive behavior, such as alcoholism, reckless driving, and violent antisocial acts. Often, one factor (commonly disruption of an important relationship) is the last straw. Serious physical disorders, especially those that are chronic and painful, play an important role in about 20% of suicides among the elderly.

Alcohol and drugs of abuse may increase disinhibition and impulsivity, as well as worsen mood, a potentially lethal combination. About 30% of people who attempt suicide have consumed alcohol before the attempt, and about one half of them were intoxicated at the time. Alcoholics are suicide-prone even when sober.

Some patients with schizophrenia commit suicide, sometimes because of depression, to which these patients are prone. The suicide method may be bizarre and violent. Attempted suicide is uncommon, although it may be the first sign of psychiatric disturbance, occurring early in schizophrenia.

People with personality disorders are prone to attempted suicide—especially emotionally immature people with a borderline or an antisocial personality disorder because they tolerate frustration poorly and react to stress impetuously with violence and aggression.

Aggression toward others is sometimes evident in suicidal behavior. Rarely, former lovers or estranged spouses are involved in murder-suicides; one person murders the other, then commits suicide.

Methods

Choice of methods is determined by many things, including cultural factors and availability as well as the seriousness of intent. Some methods (eg, jumping from heights) make survival virtually impossible, whereas others (eg, drug ingestion) may allow rescue. However, using a method that proves not to be fatal does not necessarily imply that the intent was less serious.

A bizarre method suggests an underlying psychosis. Drug ingestion is the most common method used in suicide attempts. Violent methods, such as shooting and hanging, are uncommon among attempted suicides. Some methods, such as driving over cliffs, can endanger others. Suicide by police is a bizarre form of suicide; people commit an act (eg, brandishing a weapon) that forces law enforcement agents to kill them.

For completed suicides, firearms are most commonly used by both men (74%) and women (31%), followed by hanging in men and drug ingestion in women.

Management of Suicidal Acts

A health care practitioner who foresees the likelihood of suicide in a patient is, in most jurisdictions, required to inform an empowered agency to intervene. Failure to do so can result in criminal and civil actions. Such patients should not be left alone until they are in a secure environment. They should be transported to a secure environment (often a psychiatric facility) by trained professionals (eg, ambulance, police), never by family members or friends.

Any suicidal act, regardless of whether it is a gesture or an attempt, must be taken seriously. Every person with a serious self-injury should be evaluated and treated for the physical injury. If an overdose of a potentially lethal drug is confirmed, immediate steps are taken to prevent absorption and expedite excretion, administer any available antidote, and provide supportive treatment (see Ch. 340).

Initial assessment can be done by any health care practitioner trained in the assessment and management of suicidal behavior. However, all patients require psychiatric assessment as soon as possible. A decision must be made as to whether patients need to be admitted and whether involuntary commitment or restraint is necessary. Patients with a psychotic disorder, delirium, or epilepsy and some with severe depression and an unresolved crisis should be admitted to a psychiatric unit.

After a suicide attempt, the patient may deny any problems because the severe depression that led to the suicidal act may be followed by a short-lived mood elevation. Nonetheless, the risk of later, completed suicide is high unless the patient's problems are resolved.

Psychiatric assessment identifies some of the problems that contributed to the attempt and helps the physician plan appropriate treatment. It consists of the following:

- Establishing rapport
- Understanding the suicide attempt, its background, the events preceding it, and the circumstances in which it occurred
- Appreciating the current difficulties and problems
- Thoroughly understanding personal and family relationships, which are often pertinent to the suicide attempt
- Fully assessing the patient's mental state, with particular emphasis on recognizing depression, anxiety, agitation, panic attacks, severe insomnia, other mental disorders, and alcohol or drug abuse (many of these problems require specific treatment in addition to crisis intervention)
- Interviewing close family members and friends
- Contacting the family physician

Prevention

Prevention requires identifying at-risk people and initiating appropriate interventions (see Table 167-1).

Although some attempted or completed suicides are a surprise and shock, even to close relatives and associates, clear warnings may have been given to family members, friends, or health care practitioners. Warnings are often explicit, as when patients actually discuss plans or suddenly write or change a will. However, warnings can be more subtle, as when patients make comments about having nothing to live for or being better off if dead.

On average, primary care physicians encounter ≥ 6 potentially suicidal people in their practice each year. About 77% of people who commit suicide were seen by a physician within 1 yr before killing themselves, and about 32% had been under the care of a mental health care practitioner during the preceding year. Because severe and painful physical disorders, substance abuse, and mental disorders (particularly depression) are often a factor

[**Table 167-1.** Risk Factors and Warning Signs for Suicide]

in suicide, recognizing these possible factors and initiating appropriate treatment are important contributions a physician can make to suicide prevention.

Each depressed patient should be questioned about thoughts of suicide. The fear that such inquiry may implant the idea of self-destruction is baseless. Inquiry helps the physician obtain a clearer picture of the depth of the depression, encourages constructive discussion, and conveys the physician's awareness of the patient's deep despair and hopelessness.

Even people threatening imminent suicide (eg, those who call and declare that they are going to take a lethal dose of a drug or who threaten to jump from a high height) may have some desire to live. The physician or another person to whom they appeal for help must support the desire to live. Emergency psychiatric aid for suicidal people includes the following:

- Establishing a relationship and open communication with them
- Reminding them of their identity (ie, using their name repeatedly)
- Helping sort out the problem that has caused the crisis
- Offering constructive help with the problem
- Encouraging them to take positive action
- Reminding them that family and friends care for them and want to help

Treatment of depression and risk of suicide: People with depression have a significant risk of suicide and should be carefully monitored for suicidality (suicidal behaviors and ideation). Risk of suicide may be increased early in the treatment of depression, when psychomotor retardation and indecisiveness have been ameliorated but the depressed mood is only partially lifted. When antidepressants are started or when doses are increased, a few patients experience agitation, anxiety, and increasing depression, which may increase suicidality. Recent public health warnings about the possible association between antidepressant use and suicidality in children, adolescents, and young adults have led to a significant reduction (> 20%) in antidepressant prescriptions to these populations. However, youth suicide rates increased by 14% during this period. Thus, by discouraging drug treatment of depression, these warnings may have resulted in more, not fewer, deaths by suicide. Together, these findings suggest that the best approach is to encourage treatment, but with appropriate precautions (dispensing antidepressants in sublethal amounts, giving a clear warning to patients and to family members and significant others to be alert for worsening symptoms or suicidal ideation, and, if either occurs, immediately calling the prescribing clinician or seek care elsewhere).

Effects of Suicide

Any suicidal act has a marked emotional effect on all involved. The physician, family members, and friends may feel guilt, shame, and remorse at not having prevented a suicide, as well as anger toward the deceased or others. The physician can provide valuable assistance to the deceased's family members and friends in dealing with their feelings of guilt and sorrow.

Assisted Suicide

Assisted suicide refers to the assistance given by physicians or other practitioners to people who wish to end their life. Assistance may be requests about drugs that can be saved up to provide a lethal dose, about instructions for a painless way to commit suicide, or for administration of a lethal dose of drug.

Assisted suicide is controversial and is illegal in most states in the US. Nonetheless, patients with painful, debilitating, and untreatable conditions may initiate a discussion about it with a physician. Assisted suicide may pose difficult ethical issues for physicians.