Major Depressive Disorder and Sleep Medicine

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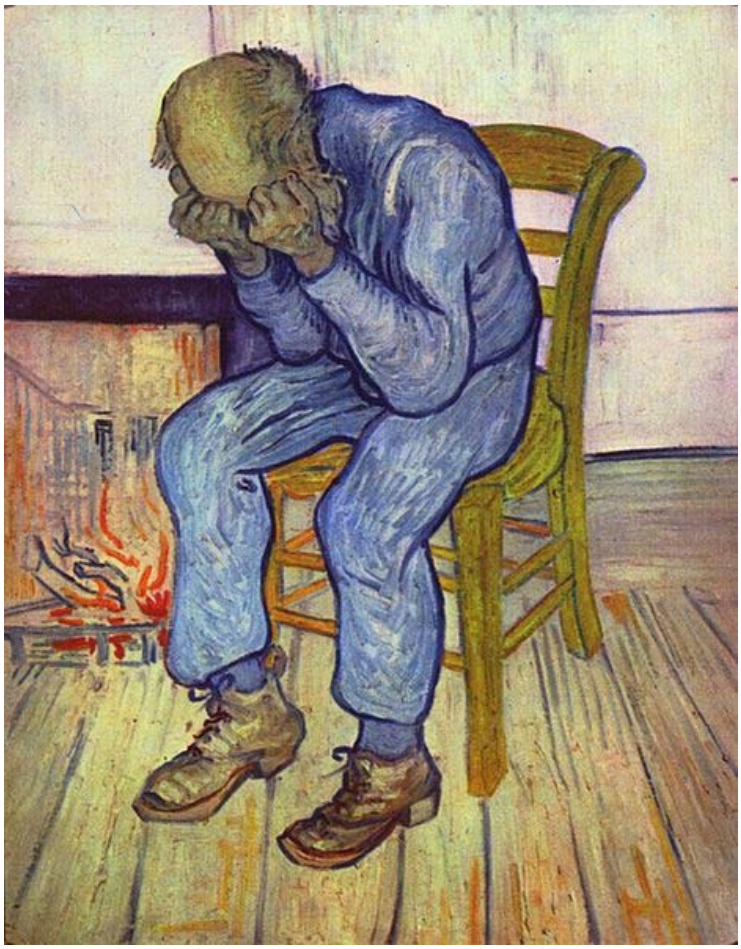
Major Depressive Disorder



Vincent van Gogh's 1890 painting
At Eternity's Gate

Major depressive disorder (**MDD**) (also known as **recurrent depressive disorder**, **clinical depression**, **major depression**, **unipolar depression**, or **unipolar disorder**) is a mental disorder characterized by an all-encompassing low mood accompanied by low self-esteem, and by loss of interest or pleasure in normally enjoyable activities. This cluster of symptoms (syndrome) was named, described and classified as one of the mood disorders in the 1980 edition of the American Psychiatric Association's diagnostic

manual. The term "depression" is ambiguous. It is often used to denote this syndrome but may refer to any or all of the mood disorders. Major depressive disorder is a disabling condition which adversely affects a person's family, work or school life, sleeping and eating habits, and general health. In the United States, around 3.4% of people with major depression commit suicide, and up to 60% of people who commit suicide had depression or another mood disorder.

The diagnosis of major depressive disorder is based on the patient's self-reported experiences, behavior reported by relatives or friends, and a mental status examination. There is no laboratory test for major depression, although physicians generally request tests for physical conditions that may cause similar symptoms. If depressive disorder is not detected in the early stages it may result in a slow recovery and affect or worsen the person's physical health. The most common time of onset is between the ages of 20 and 30 years, with a later peak between 30 and 40 years.

Typically, patients are treated with antidepressant medication and, in many cases, also receive psychotherapy or counseling although the effectiveness of medication for mild or moderate cases is questionable. Hospitalization may be necessary in cases with associated self-neglect or a significant risk of harm to self or others. A minority are treated with electroconvulsive therapy (ECT), under a short-acting general anaesthetic. The course of the disorder varies widely, from one episode lasting weeks to a lifelong disorder with recurrent major depressive episodes. Depressed individuals have shorter life expectancies than those without depression, in part because of greater susceptibility to medical illnesses and suicide. It is unclear whether or not medications affect the risk of suicide. Current and former patients may be stigmatized.

The understanding of the nature and causes of depression has evolved over the centuries, though this understanding is incomplete and has left many aspects of depression as the subject of discussion and research. Proposed causes include psychological, psycho-social, hereditary, evolutionary and biological factors. Certain types of long-term drug use can both cause and worsen depressive symptoms. Psychological treatments are based on theories of personality, interpersonal communication, and learning. Most biological theories focus on the monoamine chemicals serotonin, norepinephrine and dopamine, which are naturally present in the brain and assist communication between nerve cells.

Symptoms and signs

Major depression significantly affects a person's family and personal relationships, work or school life, sleeping and eating habits, and general health. Its impact on functioning and well-being has been equated to that of chronic medical conditions such as diabetes.

A person having a major depressive episode usually exhibits a very low mood, which pervades all aspects of life, and an inability to experience pleasure in activities that were formerly enjoyed. Depressed people may be preoccupied with, or ruminate over, thoughts and feelings of worthlessness, inappropriate guilt or regret, helplessness, hopelessness, and self-hatred. In severe cases, depressed people may have symptoms of psychosis.

These symptoms include delusions or, less commonly, hallucinations, usually unpleasant. Other symptoms of depression include poor concentration and memory (especially in those with melancholic or psychotic features), withdrawal from social situations and activities, reduced sex drive, and thoughts of death or suicide.

Insomnia is common among the depressed. In the typical pattern, a person wakes very early and cannot get back to sleep, but insomnia can also include difficulty falling asleep. Insomnia affects at least 80% of depressed people. Hypersomnia, or oversleeping, can also happen, affecting 15% of depressed people. Some antidepressants may also cause insomnia due to their stimulating effect.

A depressed person may report multiple physical symptoms such as fatigue, headaches, or digestive problems; physical complaints are the most common presenting problem in developing countries, according to the World Health Organization's criteria for depression. Appetite often decreases, with resulting weight loss, although increased appetite and weight gain occasionally occur. Family and friends may notice that the person's behavior is either agitated or lethargic.

The concept of depression is more controversial in regards to children, and depends on the view that is taken about when self-image develops and becomes fully established. Depressed children may often display an irritable mood rather than a depressed mood, and show varying symptoms depending on age and situation. Most lose interest in school and show a decline in academic performance. They may be described as clingy, demanding, dependent, or insecure. Diagnosis may be delayed or missed when symptoms are interpreted as normal moodiness. Depression may also coexist with attention-deficit hyperactivity disorder (ADHD), complicating the diagnosis and treatment of both.

Older depressed people may have cognitive symptoms of recent onset, such as forgetfulness, and a more noticeable slowing of movements. Depression often coexists with physical disorders common among the elderly, such as stroke, other cardiovascular diseases, Parkinson's disease, and chronic obstructive pulmonary disease.

Causes

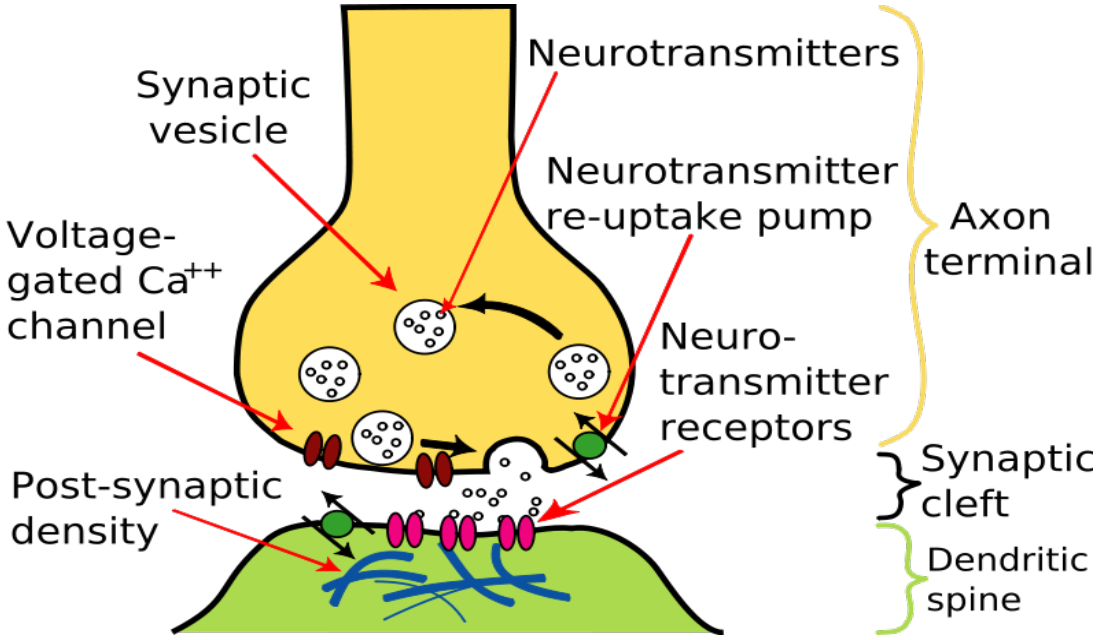
The biopsychosocial model proposes that biological, psychological, and social factors all play a role in causing depression. The diathesis–stress model specifies that depression results when a preexisting vulnerability, or diathesis, is activated by stressful life events. The preexisting vulnerability can be either genetic, implying an interaction between nature and nurture, or schematic, resulting from views of the world learned in childhood.

These interactive models have gained empirical support. For example, researchers in New Zealand took a prospective approach to studying depression, by documenting over time how depression emerged among an initially normal cohort of people. The researchers concluded that variation among the serotonin transporter (5-HTT) gene affects the chances that people who have dealt with very stressful life events will go on to experience depression. Specifically, depression may follow such events, but seems more

likely to appear in people with one or two short alleles of the 5-HTT gene. Additionally, a Swedish study estimated the heritability of depression—the degree to which individual differences in occurrence are associated with genetic differences—to be around 40% for women and 30% for men, and evolutionary psychologists have proposed that the genetic basis for depression lies deep in the history of naturally selected adaptations. A substance-induced mood disorder resembling major depression has been causally linked to long-term drug use or drug abuse, or to withdrawal from certain sedative and hypnotic drugs.

Biological

Monoamine hypothesis



Of approximately 30 neurotransmitters that have been identified, researchers have discovered associations between clinical depression and the function of three primary neurochemicals: serotonin, norepinephrine, and dopamine. Antidepressants influence the overall balance of these three neurotransmitters function within structures of the brain that regulate emotions, reactions to stress, and the physical drives of sleep, appetite, and sexuality.

Most antidepressant medications increase the levels of one or more of the monoamines—the neurotransmitters serotonin, norepinephrine and dopamine—in the synaptic cleft between neurons in the brain. Some medications affect the monoamine receptors directly.

Serotonin is hypothesized to regulate other neurotransmitter systems; decreased serotonin activity may allow these systems to act in unusual and erratic ways. According to this "permissive hypothesis", depression arises when low serotonin levels promote low levels of norepinephrine, another monoamine neurotransmitter. Some antidepressants enhance the levels of norepinephrine directly, whereas others raise the levels of dopamine, a third

monoamine neurotransmitter. These observations gave rise to the monoamine hypothesis of depression. In its contemporary formulation, the monoamine hypothesis postulates that a deficiency of certain neurotransmitters is responsible for the corresponding features of depression: "Norepinephrine may be related to alertness and energy as well as anxiety, attention, and interest in life; [lack of] serotonin to anxiety, obsessions, and compulsions; and dopamine to attention, motivation, pleasure, and reward, as well as interest in life." The proponents of this theory recommend the choice of an antidepressant with mechanism of action that impacts the most prominent symptoms. Anxious and irritable patients should be treated with SSRIs or norepinephrine reuptake inhibitors, and those experiencing a loss of energy and enjoyment of life with norepinephrine- and dopamine-enhancing drugs.

Besides the clinical observations that drugs which increase the amount of available monoamines are effective antidepressants, recent advances in psychiatric genetics indicate that phenotypic variation in central monoamine function may be marginally associated with vulnerability to depression. Despite these findings, the cause of depression is not simply monoamine deficiency. In the past two decades, research has revealed multiple limitations of the monoamine hypothesis, and its explanatory inadequacy has been highlighted within the psychiatric community. A counterargument is that the mood-enhancing effect of MAO inhibitors and SSRIs takes weeks of treatment to develop, even though the boost in available monoamines occurs within hours. Another counterargument is based on experiments with pharmacological agents that cause depletion of monoamines; while deliberate reduction in the concentration of centrally available monoamines may slightly lower the mood of unmedicated depressed patients, this reduction does not affect the mood of healthy people. An intact monoamine system is necessary for antidepressants to achieve therapeutic effectiveness, but some medications like tianeptine and opipramol have antidepressant properties despite the fact that the former is a serotonin reuptake enhancer and the latter has no effect on the monoamine system. The monoamine hypothesis, already limited, has been further oversimplified when presented to the general public as a mass marketing tool, usually phrased as a "chemical imbalance".

In 2003 a gene-environment interaction (GxE) was hypothesized to explain why life stress is a predictor for depressive episodes in some individuals, but not in others, depending on an allelic variation of the serotonin-transporter-linked promoter region (5-HTTLPR); a 2009 meta-analysis showed stressful life events was associated with depression, but found no evidence for an association with the 5-HTTLPR genotype. Another 2009 meta-analysis agreed with the latter finding. A 2010 review of studies in this area found a systematic relationship between the method used to assess environmental adversity and the results of the studies; this review also found that both 2009 meta-analyses were significantly biased toward negative studies, which used self-report measures of adversity.

Other theories

MRI scans of patients with depression have revealed a number of differences in brain structure compared to those who are not depressed. Although there is some inconsistency in the results, meta-analyses have shown there is evidence for smaller hippocampal volumes and increased numbers of hyperintensive lesions. Hyperintensities have been associated with patients with a late age of onset, and have led to the development of the theory of vascular depression.

There may be a link between depression and neurogenesis of the hippocampus, a center for both mood and memory. Loss of hippocampal neurons is found in some depressed individuals and correlates with impaired memory and dysthymic mood. Drugs may increase serotonin levels in the brain, stimulating neurogenesis and thus increasing the total mass of the hippocampus. This increase may help to restore mood and memory. Similar relationships have been observed between depression and an area of the anterior cingulate cortex implicated in the modulation of emotional behavior. One of the neurotrophins responsible for neurogenesis is brain-derived neurotrophic factor (BDNF). The level of BDNF in the blood plasma of depressed subjects is drastically reduced (more than threefold) as compared to the norm. Antidepressant treatment increases the blood level of BDNF. Although decreased plasma BDNF levels have been found in many other disorders, there is some evidence that BDNF is involved in the cause of depression and the mechanism of action of antidepressants.

There is some evidence that major depression may be caused in part by an overactive hypothalamic-pituitary-adrenal axis (HPA axis) that results in an effect similar to the neuro-endocrine response to stress. Investigations reveal increased levels of the hormone cortisol and enlarged pituitary and adrenal glands, suggesting disturbances of the endocrine system may play a role in some psychiatric disorders, including major depression. Oversecretion of corticotropin-releasing hormone from the hypothalamus is thought to drive this, and is implicated in the cognitive and arousal symptoms.

The hormone estrogen has been implicated in depressive disorders due to the increase in risk of depressive episodes after puberty, the antenatal period, and reduced rates after menopause. Conversely, the premenstrual and postpartum periods of low estrogen levels are also associated with increased risk. Sudden withdrawal of, fluctuations in or periods of sustained low levels of estrogen have been linked to significant mood lowering. Clinical recovery from depression postpartum, perimenopause, and postmenopause was shown to be effective after levels of estrogen were stabilized or restored.

Other research has explored potential roles of molecules necessary for overall cellular functioning: cytokines. The symptoms of major depressive disorder are nearly identical to those of sickness behavior, the response of the body when the immune system is fighting an infection. This raises the possibility that depression can result from a maladaptive manifestation of sickness behavior as a result of abnormalities in circulating cytokines. The involvement of pro-inflammatory cytokines in depression is strongly suggested by a

meta-analysis of the clinical literature showing higher blood concentrations of IL-6 and TNF-α in depressed subjects compared to controls.

Psychological

Various aspects of personality and its development appear to be integral to the occurrence and persistence of depression, with negative emotionality as a common precursor. Although depressive episodes are strongly correlated with adverse events, a person's characteristic style of coping may be correlated with their resilience. Additionally, low self-esteem and self-defeating or distorted thinking are related to depression. Depression is less likely to occur, as well as quicker to remit, among those who are religious. It is not always clear which factors are causes or which are effects of depression; however, depressed persons who are able to reflect upon and challenge their thinking patterns often show improved mood and self-esteem.

American psychiatrist Aaron T. Beck, following on from the earlier work of George Kelly and Albert Ellis, developed what is now known as a cognitive model of depression in the early 1960s. He proposed that three concepts underlie depression: a triad of negative thoughts composed of cognitive errors about oneself, one's world, and one's future; recurrent patterns of depressive thinking, or *schemas*; and distorted information processing. From these principles, he developed the structured technique of cognitive behavioral therapy (CBT). According to American psychologist Martin Seligman, depression in humans is similar to learned helplessness in laboratory animals, who remain in unpleasant situations when they are able to escape, but do not because they initially learned they had no control.

Attachment theory, which was developed by English psychiatrist John Bowlby in the 1960s, predicts a relationship between depressive disorder in adulthood and the quality of the earlier bond between the infant and their adult caregiver. In particular, it is thought that "the experiences of early loss, separation and rejection by the parent or caregiver (conveying the message that the child is unlovable) may all lead to insecure internal working models ... Internal cognitive representations of the self as unlovable and of attachment figures as unloving [or] untrustworthy would be consistent with parts of Beck's cognitive triad". While a wide variety of studies has upheld the basic tenets of attachment theory, research has been inconclusive as to whether self-reported early attachment and later depression are demonstrably related.

Depressed individuals often blame themselves for negative events, and, as shown in a 1993 study of hospitalized adolescents with self-reported depression, those who blame themselves for negative occurrences may not take credit for positive outcomes. This tendency is characteristic of a depressive attributional, or pessimistic explanatory style. According to Albert Bandura, a Canadian social psychologist associated with social cognitive theory, depressed individuals have negative beliefs about themselves, based on experiences of failure, observing the failure of social models, a lack of social persuasion that they can succeed, and their own somatic and emotional states including tension and

stress. These influences may result in a negative self-concept and a lack of self-efficacy; that is, they do not believe they can influence events or achieve personal goals.

An examination of depression in women indicates that vulnerability factors—such as early maternal loss, lack of a confiding relationship, responsibility for the care of several young children at home, and unemployment—can interact with life stressors to increase the risk of depression. For older adults, the factors are often health problems, changes in relationships with a spouse or adult children due to the transition to a care-giving or care-needing role, the death of a significant other, or a change in the availability or quality of social relationships with older friends because of their own health-related life changes.

The understanding of depression has also received contributions from the psychoanalytic and humanistic branches of psychology. From the classical psychoanalytic perspective of Austrian psychiatrist Sigmund Freud, depression, or *melancholia*, may be related to interpersonal loss and early life experiences. Existential therapists have connected depression to the lack of both meaning in the present and a vision of the future. The founder of humanistic psychology, American psychologist Abraham Maslow, suggested that depression could arise when people are unable to attain their needs or to self-actualize (to realize their full potential).

Social

Poverty and social isolation are associated with increased risk of mental health problems in general. Child abuse (physical, emotional, sexual, or neglect) is also associated with increased risk of developing depressive disorders later in life. Such a link has good face validity given that it is during the years of development that a child is learning how to become a social being. Abuse of the child by the caregiver is bound to distort the developing personality and create a much greater risk for depression and many other debilitating mental and emotional states. Disturbances in family functioning, such as parental (particularly maternal) depression, severe marital conflict or divorce, death of a parent, or other disturbances in parenting are additional risk factors. In adulthood, stressful life events are strongly associated with the onset of major depressive episodes. In this context, life events connected to social rejection appear to be particularly related to depression. Evidence that a first episode of depression is more likely to be immediately preceded by stressful life events than are recurrent ones is consistent with the hypothesis that people may become increasingly sensitized to life stress over successive recurrences of depression.

The relationship between stressful life events and social support has been a matter of some debate; the lack of social support may increase the likelihood that life stress will lead to depression, or the absence of social support may constitute a form of strain that leads to depression directly. There is evidence that neighborhood social disorder, for example, due to crime or illicit drugs, is a risk factor, and that a high neighborhood socioeconomic status, with better amenities, is a protective factor. Adverse conditions at work, particularly demanding jobs with little scope for decision-making, are associated

with depression, although diversity and confounding factors make it difficult to confirm that the relationship is causal.

Evolutionary

From the standpoint of evolutionary theory, major depression is hypothesized, in some instances, to increase an individual's reproductive fitness. Evolutionary approaches to depression and evolutionary psychology posit specific mechanisms by which depression may have been genetically incorporated into the human gene pool, accounting for the high heritability and prevalence of depression by proposing that certain components of depression are adaptations, such as the behaviors relating to attachment and social rank. Current behaviors can be explained as adaptations to regulate relationships or resources, although the result may be maladaptive in modern environments.

From another viewpoint, a counseling therapist may see depression, not as a biochemical illness or disorder, but as "a species-wide evolved suite of emotional programmes that are mostly activated by a perception, almost always over-negative, of a major decline in personal usefulness, that can sometimes be linked to guilt, shame or perceived rejection". This suite may have manifested in aging hunters in humans' foraging past, who were marginalized by their declining skills, and may continue to appear in alienated members of today's society. The feelings of uselessness generated by such marginalization could hypothetically prompt support from friends and kin. Additionally, in a manner analogous to that in which physical pain has evolved to hinder actions that may cause further injury, "psychic misery" may have evolved to prevent hasty and maladaptive reactions to distressing situations.

Drug and alcohol use

According to the DSM-IV, a diagnosis of mood disorder cannot be made if the cause is believed to be due to "the direct physiological effects of a substance"; when a syndrome resembling major depression is believed to be caused immediately by substance abuse or by an adverse drug reaction, it is referred to as, "substance-induced mood disturbance". Alcoholism or excessive alcohol consumption significantly increases the risk of developing major depression. Like alcohol, the benzodiazepines are central nervous system depressants; this class of medication is commonly used to treat insomnia, anxiety, and muscular spasms. Similar to alcohol, benzodiazepines increase the risk of developing major depression. This increased risk may be due in part to the effects of drugs on neurochemistry, such as decreased levels of serotonin and norepinephrine. Chronic use of benzodiazepines also can cause or worsen depression, or depression may be part of a protracted withdrawal syndrome.

Diagnosis

Clinical assessment

A diagnostic assessment may be conducted by a suitably trained general practitioner, or by a psychiatrist or psychologist, who records the person's current circumstances, biographical history, current symptoms and family history. The broad clinical aim is to formulate the relevant biological, psychological and social factors that may be impacting on the individual's mood. The assessor may also discuss the person's current ways of regulating their mood (healthy or otherwise) such as alcohol and drug use. The assessment also includes a mental state examination, which is an assessment of the person's current mood and thought content, in particular the presence of themes of hopelessness or pessimism, self-harm or suicide, and an absence of positive thoughts or plans. Specialist mental health services are rare in rural areas, and thus diagnosis and management is largely left to primary care clinicians. This issue is even more marked in developing countries. The score on a rating scale alone is insufficient to diagnose depression, but it provides an indication of the severity of symptoms for a time period, so a person who scores above a given cut-off point can be more thoroughly evaluated for a depressive disorder diagnosis. Several rating scales are used for this purpose. Screening programs have been advocated to improve detection of depression, but there is evidence that they do not improve detection rates, treatment, or outcome.

Primary care physicians and other non-psychiatrist physicians have difficulty diagnosing depression, in part because they are trained to recognize and treat physical symptoms, and depression can cause a myriad of physical (psychosomatic) symptoms. Non-psychiatrists miss two-thirds of cases and unnecessarily treat other patients.

Before diagnosing a major depressive disorder, a doctor generally performs a medical examination and selected investigations to rule out other causes of symptoms. These include blood tests measuring TSH and thyroxine to exclude hypothyroidism; basic electrolytes and serum calcium to rule out a metabolic disturbance; and a full blood count including ESR to rule out a systemic infection or chronic disease. Adverse affective reactions to medications or alcohol misuse are often ruled out, as well. Testosterone levels may be evaluated to diagnose hypogonadism, a cause of depression in men.

Subjective cognitive complaints appear in older depressed people, but they can also be indicative of the onset of a dementing disorder, such as Alzheimer's disease. Cognitive testing and brain imaging can help distinguish depression from dementia. A CT scan can exclude brain pathology in those with psychotic, rapid-onset or otherwise unusual symptoms. No biological tests confirm major depression. Investigations are not generally repeated for a subsequent episode unless there is a medical indication.

DSM-IV-TR and ICD-10 criteria

The most widely used criteria for diagnosing depressive conditions are found in the American Psychiatric Association's revised fourth edition of the *Diagnostic and*

Statistical Manual of Mental Disorders (DSM-IV-TR), and the World Health Organization's *International Statistical Classification of Diseases and Related Health Problems* (ICD-10) which uses the name *recurrent depressive disorder*. The latter system is typically used in European countries, while the former is used in the US and many other non-European nations, and the authors of both have worked towards conforming one with the other.

Major depressive disorder is classified as a mood disorder in DSM-IV-TR. The diagnosis hinges on the presence of single or recurrent major depressive episodes. Further qualifiers are used to classify both the episode itself and the course of the disorder. The category Depressive Disorder Not Otherwise Specified is diagnosed if the depressive episode's manifestation does not meet the criteria for a major depressive episode. The ICD-10 system does not use the term *major depressive disorder*, but lists very similar criteria for the diagnosis of a depressive episode (mild, moderate or severe); the term *recurrent* may be added if there have been multiple episodes without mania.

Major depressive episode

A major depressive episode is characterized by the presence of a severely depressed mood that persists for at least two weeks. Episodes may be isolated or recurrent and are categorized as mild (few symptoms in excess of minimum criteria), moderate, or severe (marked impact on social or occupational functioning). An episode with psychotic features—commonly referred to as *psychotic depression*—is automatically rated as severe. If the patient has had an episode of mania or markedly elevated mood, a diagnosis of bipolar disorder is made instead. Depression without mania is sometimes referred to as *unipolar* because the mood remains at one emotional state or "pole".

DSM-IV-TR excludes cases where the symptoms are a result of bereavement, although it is possible for normal bereavement to evolve into a depressive episode if the mood persists and the characteristic features of a major depressive episode develop. The criteria have been criticized because they do not take into account any other aspects of the personal and social context in which depression can occur. In addition, some studies have found little empirical support for the DSM-IV cut-off criteria, indicating they are a diagnostic convention imposed on a continuum of depressive symptoms of varying severity and duration: Excluded are a range of related diagnoses, including dysthymia, which involves a chronic but milder mood disturbance; recurrent brief depression, consisting of briefer depressive episodes; minor depressive disorder, whereby only some of the symptoms of major depression are present; and adjustment disorder with depressed mood, which denotes low mood resulting from a psychological response to an identifiable event or stressor.

Subtypes

The DSM-IV-TR recognizes five further subtypes of MDD, called *specifiers*, in addition to noting the length, severity and presence of psychotic features:

- **Melancholic depression** is characterized by a loss of pleasure in most or all activities, a failure of reactivity to pleasurable stimuli, a quality of depressed mood more pronounced than that of grief or loss, a worsening of symptoms in the morning hours, early morning waking, psychomotor retardation, excessive weight loss (not to be confused with anorexia nervosa), or excessive guilt.
- **Atypical depression** is characterized by mood reactivity (paradoxical anhedonia) and positivity, significant weight gain or increased appetite (comfort eating), excessive sleep or sleepiness (hypersomnia), a sensation of heaviness in limbs known as leaden paralysis, and significant social impairment as a consequence of hypersensitivity to perceived interpersonal rejection.
- **Catatonic depression** is a rare and severe form of major depression involving disturbances of motor behavior and other symptoms. Here the person is mute and almost stuporous, and either remains immobile or exhibits purposeless or even bizarre movements. Catatonic symptoms also occur in schizophrenia or in manic episodes, or may be caused by neuroleptic malignant syndrome.
- **Postpartum depression**, or **mental and behavioural disorders associated with the puerperium, not elsewhere classified**, refers to the intense, sustained and sometimes disabling depression experienced by women after giving birth. Postpartum depression has an incidence rate of 10–15% among new mothers. The DSM-IV mandates that, in order to qualify as postpartum depression, onset occur within one month of delivery. It has been said that postpartum depression can last as long as three months.
- **Seasonal affective disorder** (SAD) is a form of depression in which depressive episodes come on in the autumn or winter, and resolve in spring. The diagnosis is made if at least two episodes have occurred in colder months with none at other times, over a two-year period or longer.

Differential diagnoses

To confer major depressive disorder as the most likely diagnosis, other potential diagnoses must be considered, including dysthymia, adjustment disorder with depressed mood or bipolar disorder. Dysthymia is a chronic, milder mood disturbance in which a person reports a low mood almost daily over a span of at least two years. The symptoms are not as severe as those for major depression, although people with dysthymia are vulnerable to secondary episodes of major depression (sometimes referred to as *double depression*). Adjustment disorder with depressed mood is a mood disturbance appearing as a psychological response to an identifiable event or stressor, in which the resulting emotional or behavioral symptoms are significant but do not meet the criteria for a major depressive episode. Bipolar disorder, also known as *manic–depressive disorder*, is a condition in which depressive phases alternate with periods of mania or hypomania. Although depression is currently categorized as a separate disorder, there is ongoing debate because individuals diagnosed with major depression often experience some hypomanic symptoms, indicating a mood disorder continuum.

Other disorders need to be ruled out before diagnosing major depressive disorder. They include depressions due to physical illness, medications, and substance abuse. Depression

due to physical illness is diagnosed as a mood disorder due to a general medical condition. This condition is determined based on history, laboratory findings, or physical examination. When the depression is caused by a substance abused including a drug of abuse, a medication, or exposure to a toxin, it is then diagnosed as a substance-induced mood disorder. In such cases, a substance is judged to be etiologically related to the mood disturbance.

Schizoaffective disorder is different from major depressive disorder with psychotic features because in the schizoaffective disorder at least two weeks of delusions or hallucinations must occur in the absence of prominent mood symptoms.

Depressive symptoms may be identified during schizophrenia, delusional disorder, and psychotic disorder not otherwise specified, and in such cases those symptoms are considered associated features of these disorders, therefore, a separate diagnosis is not deemed necessary unless the depressive symptoms meet full criteria for a major depressive episode. In that case, a diagnosis of depressive disorder not otherwise specified may be made as well as a diagnosis of schizophrenia.

Some cognitive symptoms of dementia such as disorientation, apathy, difficulty concentrating and memory loss may get confused with a major depressive episode in major depressive disorder. They are especially difficult to determine in elderly patients. In such cases, the premorbid state of the patient may be helpful to differentiate both disorders. In the case of dementia, there tends to be a premorbid history of declining cognitive function. In the case of a major depressive disorder patients tend to exhibit a relatively normal premorbid state and abrupt cognitive decline associated with the depression.

Prevention

Behavioral interventions, such as interpersonal therapy, are effective at preventing new onset depression. Because such interventions appear to be most effective when delivered to individuals or small groups, it has been suggested that they may be able to reach their large target audience most efficiently through the Internet. However, an earlier meta-analysis found preventive programs with a competence-enhancing component to be superior to behaviorally oriented programs overall, and found behavioral programs to be particularly unhelpful for older people, for whom social support programs were uniquely beneficial. Additionally, the programs that best prevented depression comprised more than eight sessions, each lasting between 60 and 90 minutes; were provided by a combination of lay and professional workers; had a high-quality research design; reported attrition rates; and had a well-defined intervention. The "Coping with Depression" course (CWD) is claimed to be the most successful of psychoeducational interventions for the treatment and prevention of depression (both for its adaptability to various populations and its results), with a risk reduction of 38% in major depression and an efficacy as a treatment comparing favorably to other psychotherapies.

Management

The three most common treatments for depression are psychotherapy, medication, and electroconvulsive therapy. Psychotherapy is the treatment of choice for people under 18, while electroconvulsive therapy is only used as a last resort. Care is usually given on an outpatient basis, while treatment in an inpatient unit is considered if there is a significant risk to self or others.

Treatment options are much more limited in developing countries, where access to mental health staff, medication, and psychotherapy is often difficult. Development of mental health services is minimal in many countries; depression is viewed as a phenomenon of the developed world despite evidence to the contrary, and not as an inherently life-threatening condition. Physical exercise is recommended for management of mild depression, but it has only a moderate, statistically insignificant effect on symptoms in most cases of major depressive disorder.

Psychotherapy

Psychotherapy can be delivered, to individuals or groups, by mental health professionals, including psychotherapists, psychiatrists, psychologists, clinical social workers, counselors, and suitably trained psychiatric nurses. With more complex and chronic forms of depression, a combination of medication and psychotherapy may be used. In people under 18, according to the National Institute for Health and Clinical Excellence, medication should only be offered in conjunction with a psychological therapy, such as CBT, interpersonal therapy, or family therapy. Psychotherapy has been shown to be effective in older people. Successful psychotherapy appears to reduce the recurrence of depression even after it has been terminated or replaced by occasional booster sessions.

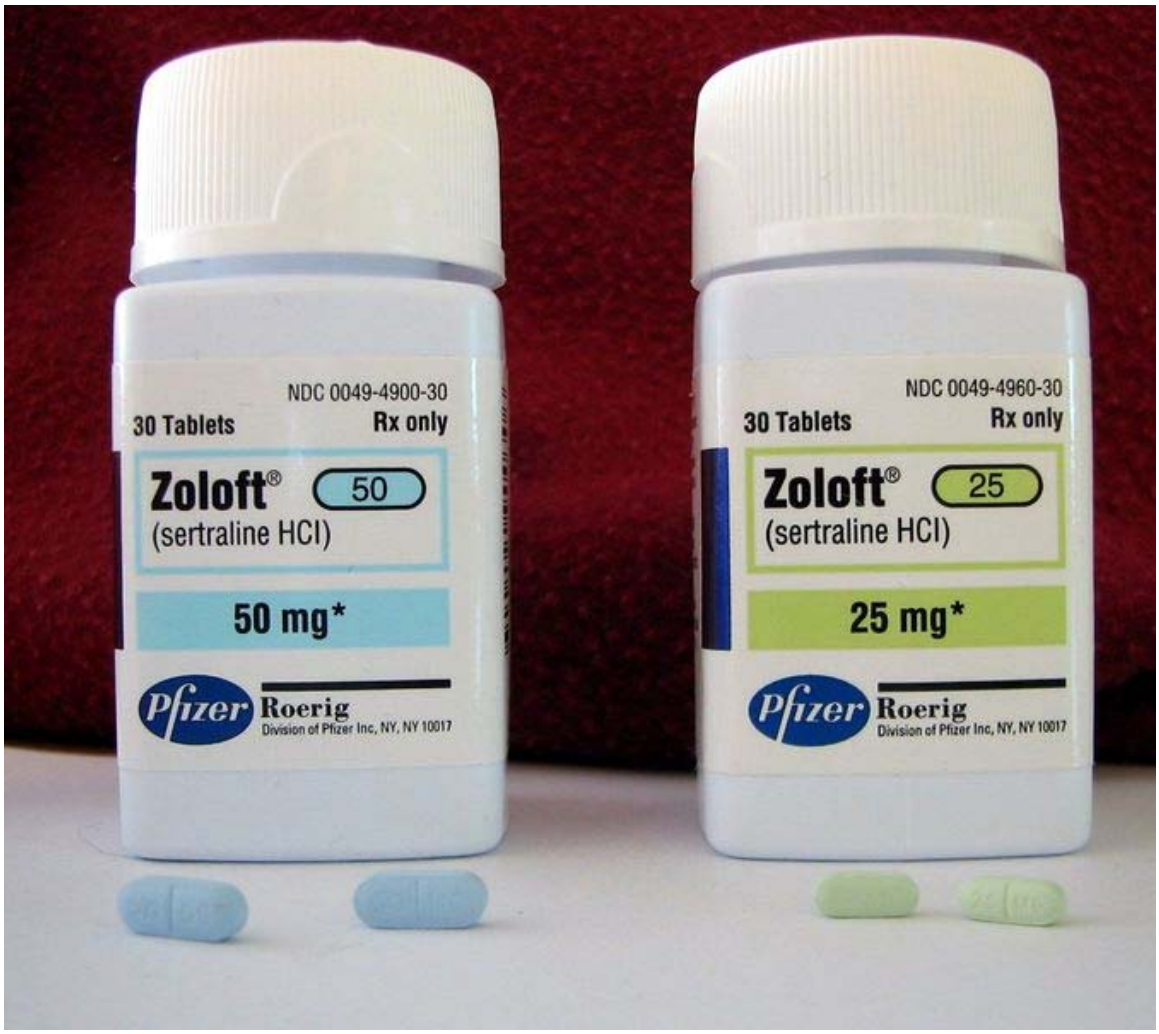
The most-studied form of psychotherapy for depression is CBT, which teaches clients to challenge self-defeating, but enduring ways of thinking (cognitions) and change counter-productive behaviours. Research beginning in the mid-1990s suggested that CBT could perform as well or better than antidepressants in patients with moderate to severe depression. CBT may be effective in depressed adolescents, although its effects on severe episodes are not definitively known. Combining fluoxetine with CBT appeared to bring no additional benefit, or, at the most, only marginal benefit. Several variables predict success for cognitive behavioral therapy in adolescents: higher levels of rational thoughts, less hopelessness, fewer negative thoughts, and fewer cognitive distortions. CBT is particularly beneficial in preventing relapse. Several variants of cognitive behavior therapy have been used in depressed patients, most notably rational emotive behavior therapy, and more recently mindfulness-based cognitive therapy.

Psychoanalysis is a school of thought, founded by Sigmund Freud, which emphasizes the resolution of unconscious mental conflicts. Psychoanalytic techniques are used by some practitioners to treat clients presenting with major depression. A more widely practiced, eclectic technique, called psychodynamic psychotherapy, is loosely based on psychoanalysis and has an additional social and interpersonal focus. In a meta-analysis of

three controlled trials of Short Psychodynamic Supportive Psychotherapy, this modification was found to be as effective as medication for mild to moderate depression.

Logotherapy, a form of existential psychotherapy developed by Austrian psychiatrist Viktor Frankl, addresses the filling of an "existential vacuum" associated with feelings of futility and meaninglessness. It is posited that this type of psychotherapy may be useful for depression in older adolescents.

Antidepressants



Zoloft (sertraline) is primarily used to treat major depression in adult outpatients. In 2007, it was the most prescribed antidepressant on the U.S. retail market, with 29,652,000 prescriptions.

The effectiveness of antidepressants are none to minimal in those with mild or moderate depression but significant in those with very severe disease. The effects of antidepressants are somewhat superior to those of psychotherapy, especially in cases of chronic major depression, although in short-term trials more patients—especially those

with less serious forms of depression—cease medication than cease psychotherapy, most likely due to adverse effects from the medication and to patients' preferences for psychological therapies over pharmacological treatments.

To find the most effective antidepressant medication with minimal side effects, the dosages can be adjusted, and if necessary, combinations of different classes of antidepressants can be tried. Response rates to the first antidepressant administered range from 50–75%, and it can take at least six to eight weeks from the start of medication to remission, when the patient is back to their normal self. Antidepressant medication treatment is usually continued for 16 to 20 weeks after remission, to minimize the chance of recurrence, and even up to one year of continuation is recommended. People with chronic depression may need to take medication indefinitely to avoid relapse.

Selective serotonin reuptake inhibitors (SSRIs) are the primary medications prescribed owing to their effectiveness, relatively mild side effects, and because they are less toxic in overdose than other antidepressants. Patients who do not respond to one SSRI can be switched to another antidepressant, and this results in improvement in almost 50% of cases. Another option is to switch to the atypical antidepressant bupropion. Venlafaxine, an antidepressant with a different mechanism of action, may be modestly more effective than SSRIs. However, venlafaxine is not recommended in the UK as a first-line treatment because of evidence suggesting its risks may outweigh benefits, and it is specifically discouraged in children and adolescents. For adolescent depression, fluoxetine and escitalopram are the two recommended choices. Antidepressants have not been found to be beneficial in children. Any antidepressant can cause low serum sodium levels (also called hyponatremia); nevertheless, it has been reported more often with SSRIs. It is not uncommon for SSRIs to cause or worsen insomnia; the sedating antidepressant mirtazapine can be used in such cases.

Monoamine oxidase inhibitors, an older class of antidepressants, have been plagued by potentially life-threatening dietary and drug interactions. They are still used only rarely, although newer and better tolerated agents of this class have been developed.

The terms "refractory depression" and "treatment-resistant depression" are used to describe cases that do not respond to adequate courses of at least two antidepressants. In many major studies, only about 35% of patients respond well to medical treatment. It may be difficult for a doctor to decide when someone has treatment-resistant depression or whether the problem is due to coexisting disorders, which are common among patients with major depression.

A team of psychologists from multiple American universities found that antidepressant drugs hardly have better effects than a placebo in cases of mild or moderate depression. The study focused on paroxetine and imipramine.

For children, adolescents, and probably young adults between 18–24 years old, there is a higher risk of both suicidal ideations and suicidal behavior in those treated with SSRIs. For adults, it is unclear whether or not SSRIs affect the risk of suicidality. One review

found no connection; another an increased risk; and a third no risk in those 25–65 years old and a decrease risk in those more than 65. Epidemiological data has found that the widespread use of antidepressants in the new "SSRI-era" is associated with a significant decline in suicide rates in most countries with traditionally high baseline suicide rates. The causality of the relationship is inconclusive. A black box warning was introduced in the United States in 2007 on SSRI and other antidepressant medications due to increased risk of suicide in patients younger than 24 years old. Similar precautionary notice revisions were implemented by the Japanese Ministry of Health.

Electroconvulsive therapy

Electroconvulsive therapy (ECT) is a procedure whereby pulses of electricity are sent through the brain via two electrodes, usually one on each temple, to induce a seizure while the patient is under a brief period of general anaesthesia. Hospital psychiatrists may recommend ECT for cases of severe major depression which have not responded to antidepressant medication or, less often, psychotherapy or supportive interventions. ECT can have a quicker effect than antidepressant therapy and thus may be the treatment of choice in emergencies such as catatonic depression where the patient has stopped eating and drinking, or where a patient is severely suicidal. ECT is probably more effective than pharmacotherapy for depression in the immediate short-term, although a landmark community-based study found much lower remission rates in routine practice. When ECT is used on its own, the relapse rate within the first six months is very high; early studies put the rate at around 50%, while a more recent controlled trial found rates of 84% even with placebos. The early relapse rate may be reduced by the use of psychiatric medications or further ECT (although the latter is not recommended by some authorities) but remains high. Common initial adverse effects from ECT include short and long-term memory loss, disorientation and headache. Although memory disturbance after ECT usually resolves within one month, ECT remains a controversial treatment, and debate on its efficacy and safety continues.

Prognosis

Major depressive episodes often resolve over time whether or not they are treated. Outpatients on a waiting list show a 10–15% reduction in symptoms within a few months, with approximately 20% no longer meeting the full criteria for a depressive disorder. The median duration of an episode has been estimated to be 23 weeks, with the highest rate of recovery in the first three months.

Studies have shown that 80% of those suffering from their first major depressive episode will suffer from at least 1 more during their life, with a lifetime average of 4 episodes. Other general population studies indicate around half those who have an episode (whether treated or not) recover and remain well, while the other half will have at least one more, and around 15% of those experience chronic recurrence. Studies recruiting from selective inpatient sources suggest lower recovery and higher chronicity, while studies of mostly outpatients show that nearly all recover, with a median episode duration

of 11 months. Around 90% of those with severe or psychotic depression, most of whom also meet criteria for other mental disorders, experience recurrence.

Recurrence is more likely if symptoms have not fully resolved with treatment. Current guidelines recommend continuing antidepressants for four to six months after remission to prevent relapse. Evidence from many randomized controlled trials indicates continuing antidepressant medications after recovery can reduce the chance of relapse by 70% (41% on placebo vs. 18% on antidepressant). The preventive effect probably lasts for at least the first 36 months of use.

Those people who experience repeated episodes of depression are required quick and ongoing treatment in order to prevent more severe, long-term depression. In some cases, people need to take medications for long periods of time or for the rest of their lives.

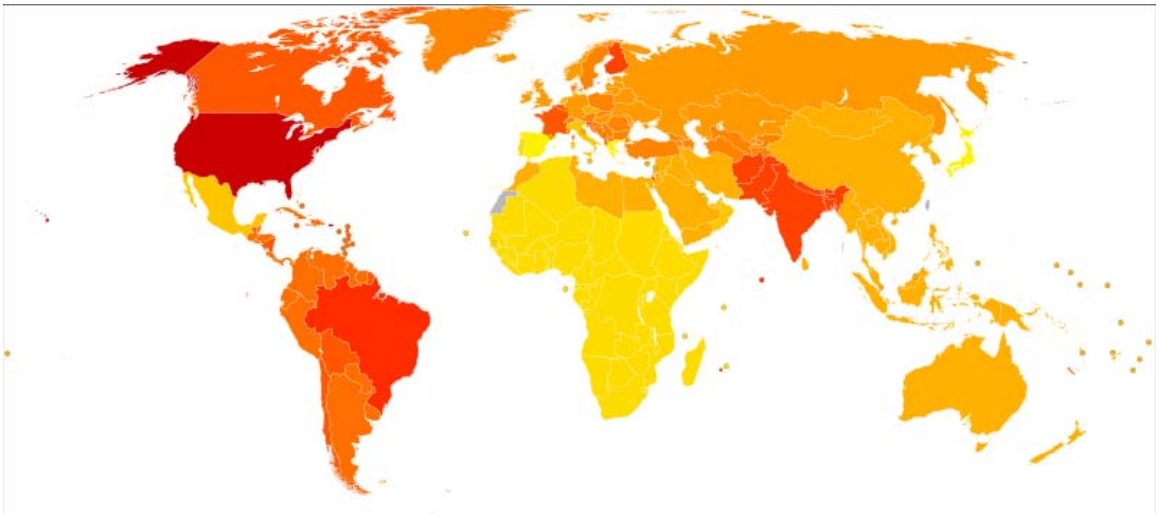
Cases when outcome is poor are associated with inappropriate treatment, severe initial symptoms that may include psychosis, early age of onset, more previous episodes, incomplete recovery after 1 year, pre-existing severe mental or medical disorder, and family dysfunction as well.

Depressed individuals have a shorter life expectancy than those without depression, in part because depressed patients are at risk of dying by suicide. However, they also have a higher rate of dying from other causes, being more susceptible to medical conditions such as heart disease. Up to 60% of people who commit suicide have a mood disorder such as major depression, and the risk is especially high if a person has a marked sense of hopelessness or has both depression and borderline personality disorder. The lifetime risk of suicide associated with a diagnosis of major depression in the US is estimated at 3.4%, which averages two highly disparate figures of almost 7% for men and 1% for women (although suicide attempts are more frequent in women). The estimate is substantially lower than a previously accepted figure of 15% which had been derived from older studies of hospitalized patients.

Depression is often associated with unemployment and poverty. Major depression is currently the leading cause of disease burden in North America and other high-income countries, and the fourth-leading cause worldwide. In the year 2030, it is predicted to be the second-leading cause of disease burden worldwide after HIV, according to the World Health Organization. Delay or failure in seeking treatment after relapse, and the failure of health professionals to provide treatment, are two barriers to reducing disability.

Epidemiology

Prevalence



Age-standardised disability-adjusted life year (DALY) rates of unipolar depressive disorders by country (per 100,000 inhabitants) in 2004.

Depression is a major cause of morbidity worldwide. Lifetime prevalence varies widely, from 3% in Japan to 17% in the US. In most countries the number of people who would suffer from depression during their lives falls within an 8–12% range. In North America the probability of having a major depressive episode within a year-long period is 3–5% for males and 8–10% for females. Population studies have consistently shown major depression to be about twice as common in women as in men, although it is unclear why this is so, and whether factors unaccounted for are contributing to this. The relative increase in occurrence is related to pubertal development rather than chronological age, reaches adult ratios between the ages of 15 and 18, and appears associated with psychosocial more than hormonal factors.

People are most likely to suffer their first depressive episode between the ages of 30 and 40, and there is a second, smaller peak of incidence between ages 50 and 60. The risk of major depression is increased with neurological conditions such as stroke, Parkinson's disease, or multiple sclerosis and during the first year after childbirth. It is also more common after cardiovascular illnesses, and is related more to a poor outcome than to a better one. Studies conflict on the prevalence of depression in the elderly, but most data suggest there is a reduction in this age group. Depressive disorder are most common to observe in urban than in rural population and the prevalence is in groups with higher socioeconomic factors i.e. homeless people

Comorbidity

Major depression frequently co-occurs with other psychiatric problems. The 1990–92 *National Comorbidity Survey* (US) reports that 51% of those with major depression also

suffer from lifetime anxiety. Anxiety symptoms can have a major impact on the course of a depressive illness, with delayed recovery, increased risk of relapse, greater disability and increased suicide attempts. American neuroendocrinologist Robert Sapolsky similarly argues that the relationship between stress, anxiety, and depression could be measured and demonstrated biologically. There are increased rates of alcohol and drug abuse and particularly dependence, and around a third of individuals diagnosed with ADHD develop comorbid depression. Post-traumatic stress disorder and depression often co-occur.

Depression and pain often co-occur. This may be for the simple reason that is obviously depressing to be in pain, especially if it is chronic or cannot be controlled. This also fits with Seligman's theory of learned helplessness. One or more pain symptoms is present in 65% of depressed patients, and anywhere from five to 85% of patients with pain will be suffering from depression, depending on the setting; there is a lower prevalence in general practice, and higher in specialty clinics. The diagnosis of depression is often delayed or missed, and the outcome worsens. The outcome can also obviously worsen if the depression is noticed but completely misunderstood

Depression is also associated with a 1.5- to 2-fold increased risk of cardiovascular disease, independent of other known risk factors, and is itself linked directly or indirectly to risk factors such as smoking and obesity. People with major depression are less likely to follow medical recommendations for treating cardiovascular disorders, which further increases their risk. In addition, cardiologists may not recognize underlying depression that complicates a cardiovascular problem under their care.

History

The Ancient Greek physician Hippocrates described a syndrome of melancholia as a distinct disease with particular mental and physical symptoms; he characterized all "fears and despondencies, if they last a long time" as being symptomatic of the ailment. It was a similar but far broader concept than today's depression; prominence was given to a clustering of the symptoms of sadness, dejection, and despondency, and often fear, anger, delusions and obsessions were included.

The term *depression* itself was derived from the Latin verb *deprimere*, "to press down". From the 14th century, "to depress" meant to subjugate or to bring down in spirits. It was used in 1665 in English author Richard Baker's *Chronicle* to refer to someone having "a great depression of spirit", and by English author Samuel Johnson in a similar sense in 1753. The term also came in to use in physiology and economics. An early usage referring to a psychiatric symptom was by French psychiatrist Louis Delasiauve in 1856, and by the 1860s it was appearing in medical dictionaries to refer to a physiological and metaphorical lowering of emotional function. Since Aristotle, melancholia had been associated with men of learning and intellectual brilliance, a hazard of contemplation and creativity. The newer concept abandoned these associations and through the 19th century, became more associated with women.

Although *melancholia* remained the dominant diagnostic term, *depression* gained increasing currency in medical treatises and was a synonym by the end of the century; German psychiatrist Emil Kraepelin may have been the first to use it as the overarching term, referring to different kinds of melancholia as *depressive states*.

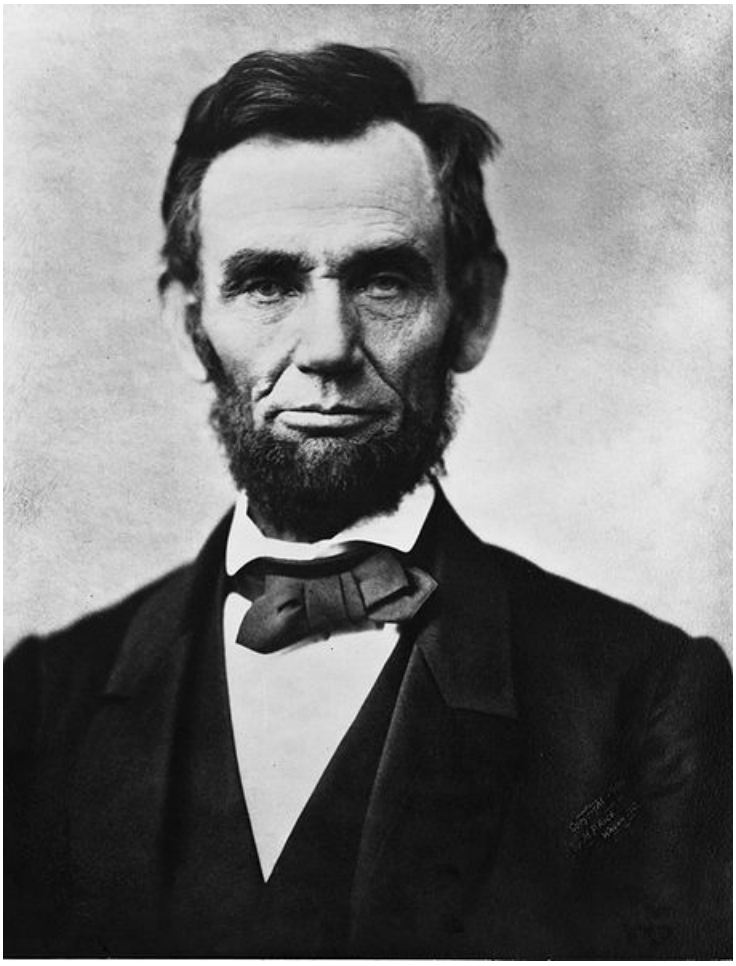
Sigmund Freud likened the state of melancholia to mourning in his 1917 paper *Mourning and Melancholia*. He theorized that objective loss, such as the loss of a valued relationship through death or a romantic break-up, results in subjective loss as well; the depressed individual has identified with the object of affection through an unconscious, narcissistic process called the *libidinal cathexis* of the ego. Such loss results in severe melancholic symptoms more profound than mourning; not only is the outside world viewed negatively, but the ego itself is compromised. The patient's decline of self-perception is revealed in his belief of his own blame, inferiority, and unworthiness. He also emphasized early life experiences as a predisposing factor. Meyer put forward a mixed social and biological framework emphasizing *reactions* in the context of an individual's life, and argued that the term *depression* should be used instead of *melancholia*. The first version of the DSM (DSM-I, 1952) contained *depressive reaction* and the DSM-II (1968) *depressive neurosis*, defined as an excessive reaction to internal conflict or an identifiable event, and also included a depressive type of manic-depressive psychosis within Major affective disorders.

In the mid-20th century, researchers theorized that depression was caused by a chemical imbalance in neurotransmitters in the brain, a theory based on observations made in the 1950s of the effects of reserpine and isoniazid in altering monoamine neurotransmitter levels and affecting depressive symptoms.

The term *Major depressive disorder* was introduced by a group of US clinicians in the mid-1970s as part of proposals for diagnostic criteria based on patterns of symptoms (called the "Research Diagnostic Criteria", building on earlier Feighner Criteria), and was incorporated in to the DSM-III in 1980. To maintain consistency the ICD-10 used the same criteria, with only minor alterations, but using the DSM diagnostic threshold to mark a *mild depressive episode*, adding higher threshold categories for moderate and severe episodes. The ancient idea of *melancholia* still survives in the notion of a melancholic subtype.

The new definitions of depression were widely accepted, albeit with some conflicting findings and views. There have been some continued empirically based arguments for a return to the diagnosis of melancholia. There has been some criticism of the expansion of coverage of the diagnosis, related to the development and promotion of antidepressants and the biological model since the late 1950s.

Society and culture



Former American president Abraham Lincoln suffered from "melancholy", a condition which now may be referred to as clinical depression.

People's conceptualizations of depression vary widely, both within and among cultures. "Because of the lack of scientific certainty," one commentator has observed, "the debate over depression turns on questions of language. What we call it—'disease,' 'disorder,' 'state of mind'—affects how we view, diagnose, and treat it." There are cultural differences in the extent to which serious depression is considered an illness requiring personal professional treatment, or is an indicator of something else, such as the need to address social or moral problems, the result of biological imbalances, or a reflection of individual differences in the understanding of distress that may reinforce feelings of powerlessness, and emotional struggle.

The diagnosis is less common in some countries, such as China. It has been argued that the Chinese traditionally deny or somatize emotional depression (although since the early 1980s the Chinese denial of depression may have modified drastically). Alternatively, it may be that Western cultures reframe and elevate some expressions of human distress to disorder status. Australian professor Gordon Parker and others have argued that the

Western concept of depression "medicalizes" sadness or misery. Similarly, Hungarian-American psychiatrist Thomas Szasz and others argue that depression is a metaphorical illness that is inappropriately regarded as an actual disease. There has also been concern that the DSM, as well as the field of descriptive psychiatry that employs it, tends to reify abstract phenomena such as depression, which may in fact be social constructs. American archetypal psychologist James Hillman writes that depression can be healthy for the soul, insofar as "it brings refuge, limitation, focus, gravity, weight, and humble powerlessness." Hillman argues that therapeutic attempts to eliminate depression echo the Christian theme of resurrection, but have the unfortunate effect of demonizing a soulful state of being.

Historical figures were often reluctant to discuss or seek treatment for depression due to social stigma about the condition, or due to ignorance of diagnosis or treatments. Nevertheless, analysis or interpretation of letters, journals, artwork, writings or statements of family and friends of some historical personalities has led to the presumption that they may have had some form of depression. People who may have had depression include English author Mary Shelley, American-British writer Henry James, and American president Abraham Lincoln. Some well-known contemporary people with possible depression include Canadian songwriter Leonard Cohen and American playwright and novelist Tennessee Williams. Some pioneering psychologists, such as Americans William James and John B. Watson, dealt with their own depression.

There has been a continuing discussion of whether neurological disorders and mood disorders may be linked to creativity, a discussion that goes back to Aristotelian times. British literature gives many examples of reflections on depression. English philosopher John Stuart Mill experienced a several-months-long period of what he called "a dull state of nerves", when one is "unsusceptible to enjoyment or pleasurable excitement; one of those moods when what is pleasure at other times, becomes insipid or indifferent". He quoted English poet Samuel Taylor Coleridge's "Dejection" as a perfect description of his case: "A grief without a pang, void, dark and drear, / A drowsy, stifled, unimpassioned grief, / Which finds no natural outlet or relief / In word, or sigh, or tear." English writer Samuel Johnson used the term "the black dog" in the 1780s to describe his own depression, and it was subsequently popularized by depression sufferer former British Prime Minister Sir Winston Churchill.

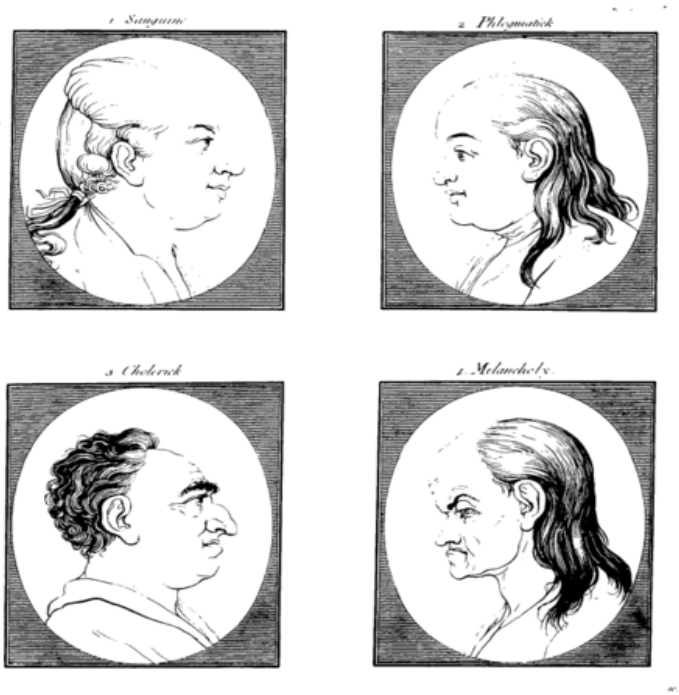
Social stigma of major depression is widespread, and contact with mental health services reduces this only slightly. Public opinions on treatment differ markedly to those of health professionals; alternative treatments are held to be more helpful than pharmacological ones, which are viewed poorly. In the UK, the Royal College of Psychiatrists and the Royal College of General Practitioners conducted a joint Five-year Defeat Depression campaign to educate and reduce stigma from 1992 to 1996; a MORI study conducted afterwards showed a small positive change in public attitudes to depression and treatment.

Chapter 2

History of Depression

What was previously known as melancholia and is now known as *clinical depression*, *major depression*, or simply *depression* and commonly referred to as major depressive disorder by many health care professionals, has a long history, with similar conditions being described at least as far back as classical times.

Prehistory to medieval periods



The four temperaments (clockwise from top left; sanguine; phlegmatic; melancholic; choleric) according to an ancient theory of mental states

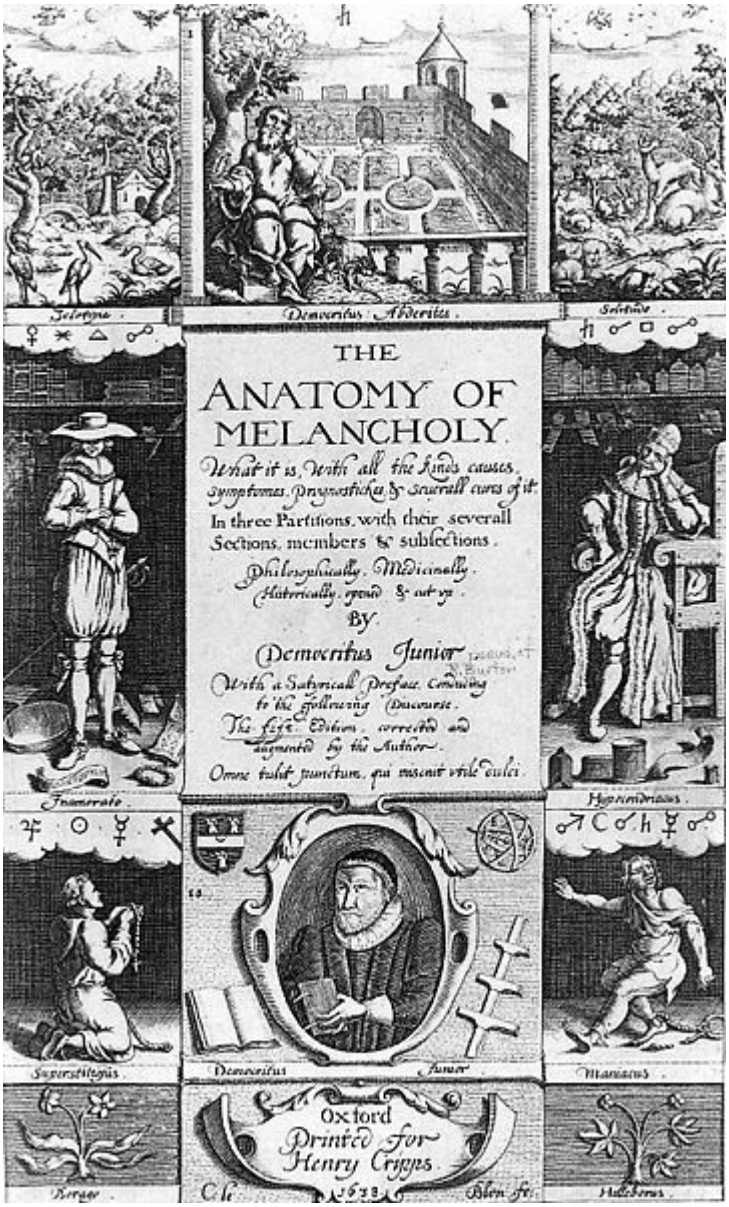
In Ancient Greece, disease was thought due to an imbalance in the four basic bodily fluids, or *humors*. Personality types were similarly thought to be determined by the dominant humor in a particular person. Derived from the Ancient Greek *melas*, "black", and *kholé*, "bile", melancholia was described as a distinct disease with particular mental and physical symptoms by Hippocrates in his *Aphorisms*, where he characterized all "fears and despondencies, if they last a long time" as being symptomatic of the ailment.

Aretaeus of Cappadocia later noted that sufferers were "dull or stern; dejected or unreasonably torpid, without any manifest cause". The humoral theory fell out of favor but was revived in Rome by Galen. Melancholia was a far broader concept than today's depression; prominence was given to a clustering of the symptoms of sadness, dejection, and despondency, and often fear, anger, delusions and obsessions were included.

Influenced by Greek and Roman texts, physicians in the Persian and then the Muslim world developed ideas about melancholia during the Islamic Golden Age. Ishaq ibn Imran (d. 908) combined the concepts of melancholia and phrenitis. The 11th century Persian physician Avicenna described melancholia as a depressive type of mood disorder in which the person may become suspicious and develop certain types of phobias.

His work, *The Canon of Medicine*, became the standard of medical thinking in Europe alongside those of Hippocrates and Galen. Moral and spiritual theories also prevailed, and in the Christian environment of medieval Europe, a malaise called *acedia* (sloth or absence of caring) was identified, involving low spirits and lethargy typically linked to isolation.

17th to 19th centuries



Frontispiece of the 1638 edition of *The Anatomy of Melancholy*

The seminal scholarly work of the 17th century was English scholar Robert Burton's book, *The Anatomy of Melancholy*, drawing on numerous theories and the author's own experiences. Burton suggested that melancholy could be combated with a healthy diet, sufficient sleep, music, and "meaningful work", along with talking about the problem with a friend.

During the 18th century, the humoral theory of melancholia was increasingly challenged by mechanical and electrical explanations; references to dark and gloomy states gave way to ideas of slowed circulation and depleted energy. German physician Johann Christian

Heinroth, however, argued melancholia was a disturbance of the soul due to moral conflict within the patient.

Eventually, various authors proposed up to 30 different subtypes of melancholia, and alternative terms were suggested and discarded. Hypochondria came to be seen as a separate disorder. *Melancholia* and *Melancholy* had been used interchangeably until the 19th century, but the former came to refer to a pathological condition and the latter to a temperament.

The term *depression* was derived from the Latin verb *deprimere*, "to press down". From the 14th century, "to depress" meant to subjugate or to bring down in spirits. It was used in 1665 in English author Richard Baker's *Chronicle* to refer to someone having "a great depression of spirit", and by English author Samuel Johnson in a similar sense in 1753. The term also came in to use in physiology and economics.

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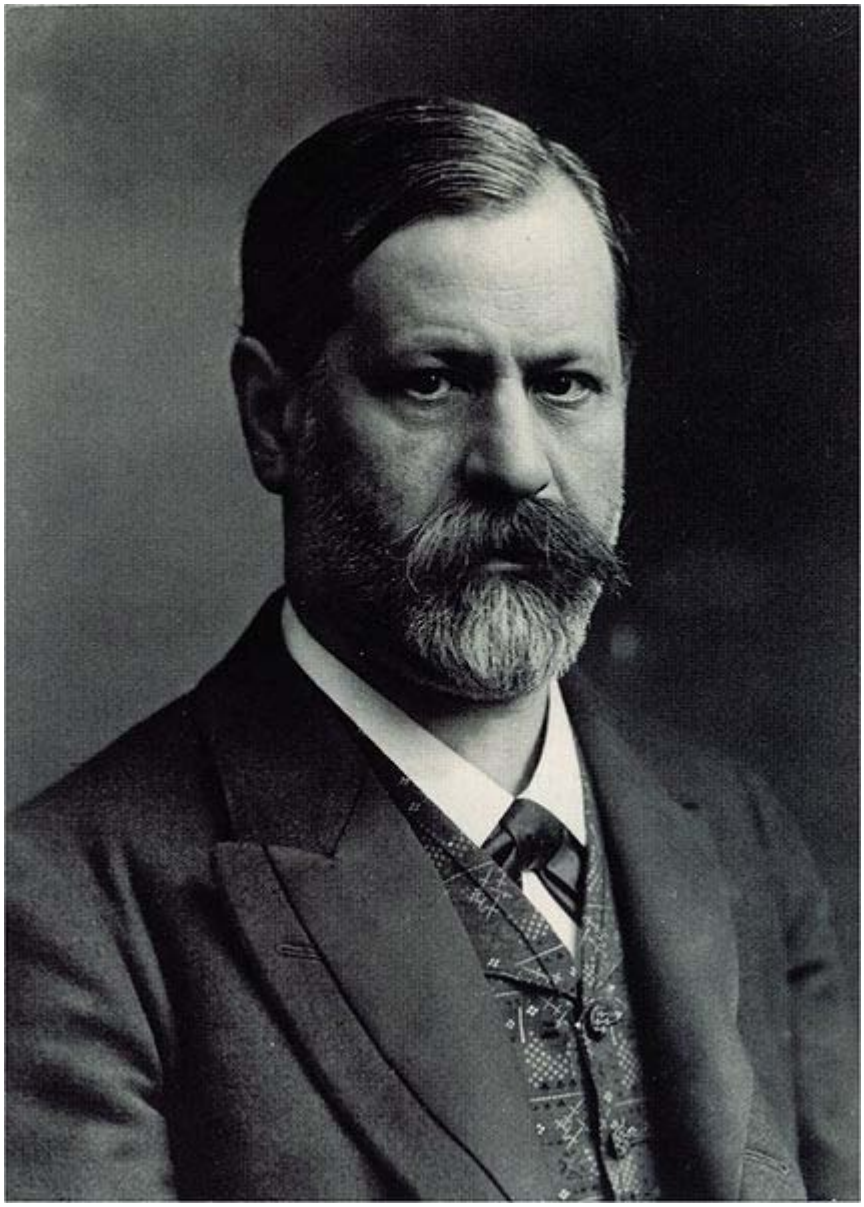
20th and 21st centuries

The influential system put forward by Kraepelin unified nearly all types of mood disorder into *manic–depressive insanity*. Kraepelin worked from an assumption of underlying brain pathology, but also promoted a distinction between endogenous (internally caused) and exogenous (externally caused) types.

German psychiatrist Kurt Schneider coined the terms *endogenous depression* and *reactive depression* in 1920, the latter referring to reactivity in mood and not *reaction* to outside events, and therefore frequently misinterpreted. The division was challenged in 1926 by Edward Mapother who found no clear distinction between the types.

The unitarian view became more popular in the United Kingdom, while the binary view held sway in the US, influenced by the work of Swiss psychiatrist Adolf Meyer and before him Sigmund Freud, the father of psychoanalysis.



Sigmund Freud argued that depression, or melancholia, could result from loss and is more severe than mourning.

Freud had likened the state of melancholia to mourning in his 1917 paper *Mourning and Melancholia*. He theorized that objective loss, such as the loss of a valued relationship through death or a romantic break-up, results in subjective loss as well; the depressed individual has identified with the object of affection through an unconscious, narcissistic process called the *libidinal cathexis* of the ego.

Such loss results in severe melancholic symptoms more profound than mourning; not only is the outside world viewed negatively, but the ego itself is compromised. The patient's decline of self-perception is revealed in his belief of his own blame, inferiority, and unworthiness. He also emphasized early life experiences as a predisposing factor.

Meyer put forward a mixed social and biological framework emphasizing *reactions* in the context of an individual's life, and argued that the term *depression* should be used instead of *melancholia*.

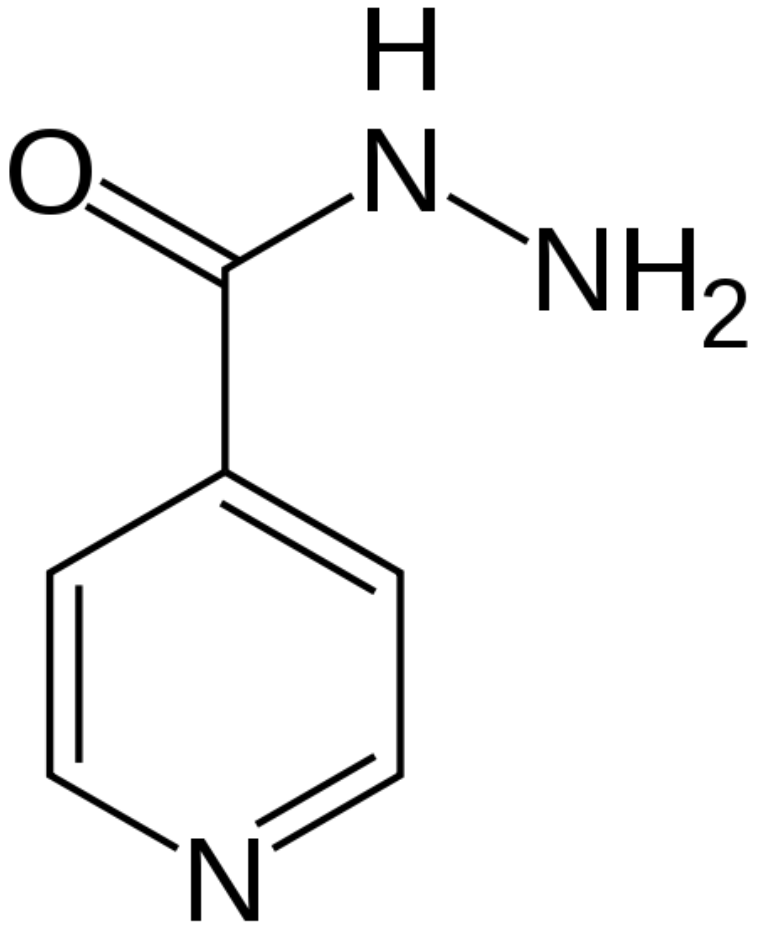
The DSM-I (1952) contained *depressive reaction* and the DSM-II (1968) *depressive neurosis*, defined as an excessive reaction to internal conflict or an identifiable event, and also included a depressive type of manic-depressive psychosis within Major affective disorders.

In the mid-20th century, other psychodynamic theories were proposed. Existential and humanistic theories represented a forceful affirmation of individualism. Austrian existential psychiatrist Viktor Frankl connected depression to feelings of futility and meaninglessness. Frankl's logotherapy addressed the filling of an "existential vacuum" associated with such feelings, and may be particularly useful for depressed adolescents.

American existential psychologist Rollo May hypothesized that "depression is the inability to construct a future". In general, May wrote, "depression ... occur[s] more in the dimension of time than in space," and the depressed individual fails to look ahead in time properly. Thus the "focusing upon some point in time *outside* the depression ... gives the patient a perspective, a view on high so to speak; and this may well break the chains of the ... depression."

Humanistic psychologists argued that depression resulted from an incongruity between society and the individual's innate drive to self-actualize, or to realize one's full potential. American humanistic psychologist Abraham Maslow theorized that depression is especially likely to arise when the world precludes a sense of "richness" or "totality" for the self-actualizer.

A half century ago, diagnosed depression was either endogenous (melancholic), considered a biological condition, or reactive (neurotic), a reaction to stressful events. Debate has persisted for most of the 20th century over whether a unitary or binary model of depression is a truer reflection of the syndrome; in the former, there is a continuum of depression ranked only by severity and the result of a "psychobiological final common pathway", whereas the latter conceptualizes a distinction between biological and reactive depressive syndromes. The publishing of DSM-III saw the unitarian model gain a more universal acceptance.



Isoniazid was the first compound to be called an antidepressant

In the mid-20th century, researchers theorized that depression was caused by a chemical imbalance in neurotransmitters in the brain, a theory based on observations made in the 1950s of the effects of reserpine and isoniazid in altering monoamine neurotransmitter levels and affecting depressive symptoms. During the 1960s and 70s, manic-depression came to refer to just one type of mood disorder (now most commonly known as bipolar disorder) which was distinguished from (unipolar) depression. The terms unipolar and bipolar had been coined by German psychiatrist Karl Kleist.

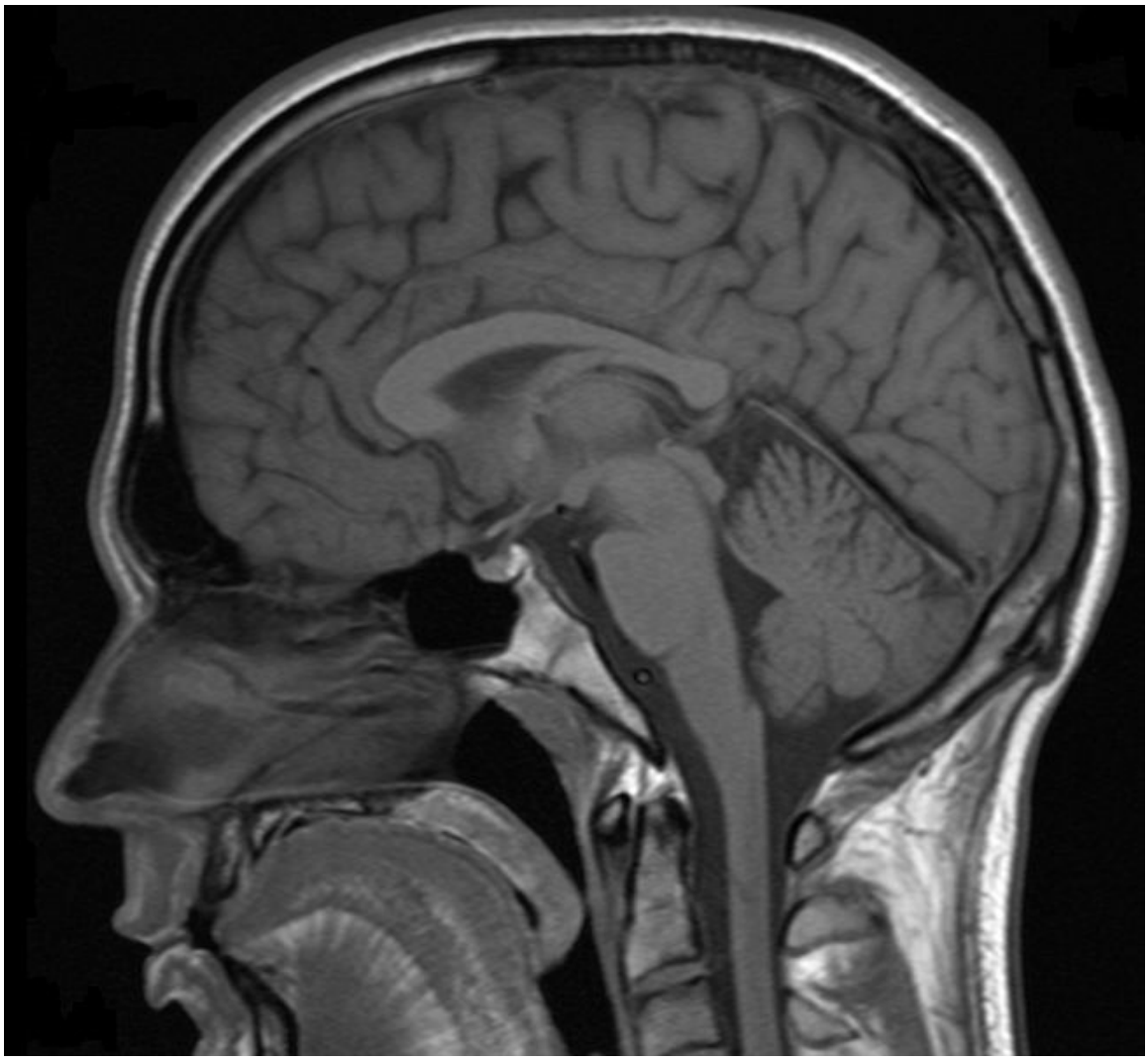
The term *Major depressive disorder* was introduced by a group of US clinicians in the mid-1970s as part of proposals for diagnostic criteria based on patterns of symptoms (called the Research Diagnostic Criteria, building on earlier Feighner Criteria), and was incorporated in to the DSM-III in 1980. To maintain consistency the ICD-10 used the same criteria, with only minor alterations, but using the DSM diagnostic threshold to mark a *mild depressive episode*, adding higher threshold categories for moderate and severe episodes.

The ancient idea of *melancholia* still survives in the notion of a melancholic subtype. The new definitions of depression were widely accepted, albeit with some conflicting findings and views, and the nomenclature continues in DSM-IV-TR, the latest version, published in 2000.

There have been some continued empirical arguments for a return to the diagnosis of melancholia. There has been some criticism of the expansion of coverage of the diagnosis, related to the development and promotion of antidepressants and the biological model since the late 1950s.

Chapter 3

Depression (Differential Diagnoses)



Neuroimaging can be a valuable tool in the diagnostic work-up of various psychiatric disorders including depression.

Depression, one of the most commonly diagnosed psychiatric disorders. is being diagnosed in increasing numbers in various segments of the population worldwide.

Depression in the United States alone affects 17.6 million Americans each year or 1 in 6 people. Depressed patients are at increased risk of type 2 diabetes, cardiovascular disease and suicide. Within the next twenty years depression is expected to become the second leading cause of disability worldwide and the leading cause in high-income nations, including the United States. In approximately 75% of completed suicides the individuals had seen a physician within the prior year before their death, 45%-66% within the prior month. Approximately 33% - 41% of those who completed suicide had contact with mental health services in the prior year, 20% within the prior month.

There are many psychiatric and medical conditions that may mimic some or all of the symptoms of depression, or may occur comorbid to it. A disorder either psychiatric or medical that shares symptoms and characteristics of another disorder, and may be the true cause of the presenting symptoms is known as a differential diagnosis.

Many ostensibly psychiatric disorders such as depression are diagnosed by allied health professionals with little or no medical training, and are made on the basis of presenting symptoms without proper consideration of the underlying cause, adequate screening of differential diagnoses is often not conducted. According to one study "non-medical mental health care providers may be at increased risk of not recognizing masked medical illnesses in their patients."

Misdiagnosis or missed diagnoses may lead to lack of treatment or ineffective and potentially harmful treatment which may worsen the underlying causative disorder. Conservative estimates are, that 10% of all psychological symptoms may be due to medical reasons, with the results of one study, suggesting that about 50% of individuals with a serious mental illness "have general medical conditions that are largely undiagnosed and untreated and may cause or exacerbate psychiatric symptoms."

In a case of misdiagnosed depression recounted in Newsweek, a writer received treatment for depression for years; during the last 10 years of her depression the symptoms worsened resulting in multiple suicide attempts and psychiatric hospitalizations. When an MRI finally was performed it showed the presence of a tumor. She was however told by a neurologist that it was benign. After a worsening of symptoms, upon the second opinion of another neurologist, the tumor was removed. After the surgery she no longer suffered from "depression".

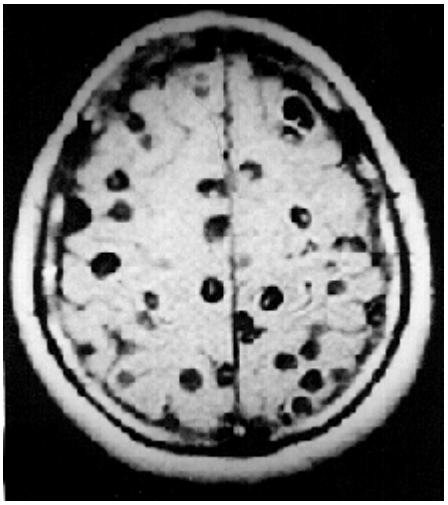
Autoimmune disorders

- Celiac disease; is an autoimmune disorder in which the body is unable to digest gluten, found in various grains such as rye and barley. Current research has shown its neuropsychiatric symptoms may manifest without the gastrointestinal symptoms.

  "However, more recent studies have emphasized that a wider spectrum of neurologic syndromes may be the presenting extraintestinal manifestation of gluten sensitivity with or without intestinal pathology."

- Lupus: Systemic lupus erythematosus (SLE), is a chronic autoimmune connective tissue disease that can affect any part of the body. Lupus can cause or worsen depression.

Bacterial-viral-parasitic infection



MRI brain scan: Neurocysticercosis

- Lyme disease; is a bacterial infection caused by Borrelia burgdorferi, a spirochete bacterium transmitted by the Deer tick (ixodes scapulari). Lyme disease is one of a group of diseases which have earned the name the "great imitator" for their propensity to mimic the symptoms of a wide variety of medical and neuropsychiatric disorders. Lyme disease is an underdiagnosed illness, partially as a result of the complexity and unreliability of serologic testing.

  "Because of the rapid rise of Lyme borreliosis nationwide and the need for antibiotic treatment to prevent severe neurologic damage, mental health professionals need to be aware of its possible psychiatric presentations.

- Syphilis; the prevalence of which is on the rise, is another of the "great imitators", which if left untreated can progress to neurosyphilis and affect the brain, can present with solely neuropsychiatric symptoms. "This case emphasises that neurosyphilis still has to be considered in the differential diagnosis within the context of psychiatric conditions and diseases. Owing to current epidemiological data and difficulties in diagnosing syphilis, routine screening tests in the psychiatric field are necessary."
- Neurocysticercosis (NCC): is an infection of the brain or spinal cord caused by the larval stage of the pork tapeworm, *Taenia solium*. NCC is the most common helminthic (parasitic worm) infestation of the central nervous system worldwide. Humans develop cysticercosis when they ingest eggs of the pork tapeworm via contact with contaminated fecal matter or eating infected vegetables or undercooked pork. "While cysticercosis is endemic in Latin America, it is an emerging disease with increased prevalence in the United States." "The rate of

depression in those with neurocysticercosis is higher than in the general population."

- Toxoplasmosis; is an infection caused by *Toxoplasma gondii* an intracellular protozoan parasite. Humans can be infected in 3 different ways: ingestion of tissue cysts, ingestion of oocysts, or in utero infection with tachyzoites. One of the prime methods for transmission to humans is contact with the feces of the host species, the domesticated cat. Toxoplasma gondii infects approximately 30% of the world's human population, but causes overt clinical symptoms in only a small segment of those infected. Exposure to Toxoplasma gondii (seropositivity) without developing Toxoplasmosis has been proven to alter various characteristics of human behavior as well as being a causative factor in some cases of depression, in addition, studies have linked seropositivity with an increased rate of suicide
- West Nile virus (WNV); which can cause encephalitis has been reported to be a causal factor in developing depression in 31% of those infected in a study conducted in Houston, Texas and reported to the Center for Disease Control (CDC). The primary vectors for disease transmission to humans are various species of mosquito. WNV which is endemic to Southern Europe, Africa the Middle East and Asia was first identified in the United States in 1999. Between 1999 and 2006, 20,000 cases of confirmed symptomatic WNV were reported in the United States, with estimates of up to 1 million being infected. "WNV is now the most common cause of epidemic viral encephalitis in the United States, and it will likely remain an important cause of neurological disease for the foreseeable future."

Blood disorders

- Anemia: is a decrease in normal number of red blood cells (RBCs) or less than the normal quantity of hemoglobin in the blood. Depressive symptoms are associated with anemia in a general population of older persons living in the community.

Chronic fatigue syndrome

Between 1 and 4 million Americans are believed to have Chronic Fatigue Syndrome (CFS), yet only 50% have consulted a physician for symptoms of CFS. In addition individuals with CFS symptoms often have an undiagnosed medical or psychiatric disorder such as diabetes, thyroid disease or substance abuse. CFS, at one time considered to be psychosomatic in nature, is now considered to be a valid medical condition in which early diagnosis and treatment can aid in alleviating or completely resolving symptoms. While frequently misdiagnosed as depression, differences have been noted in rate of cerebral blood flow.

CFS is underdiagnosed in more than 80% of the people who have it; at the same time, it is often misdiagnosed as depression.

Dietary disorders

- Fructose malabsorption and lactose intolerance; deficient fructose transport by the duodenum, or by the deficiency of the enzyme, lactase in the mucosal lining, respectively. As a result of this malabsorption the saccharides reach the colon and are digested by bacteria which convert them to short chain fatty acids, CO_2, and H_2. Approximately 50% of those afflicted exhibit the physical signs of irritable bowel syndrome

  "Fructose malabsorption may play a role in the development of depressed mood. Fructose malabsorption should be considered in patients with symptoms of major depression...."
  "Fructose and sorbitol reduced diet in subjects with fructose malabsorption does not only reduce gastrointestinal symptoms but also improves mood and early signs of depression."

Endocrine system disorders

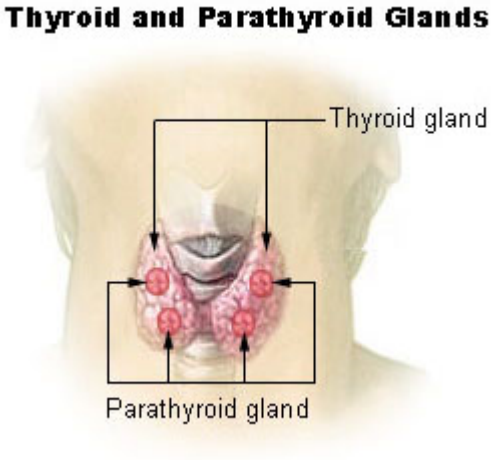
Dysregulation of the endocrine system may present with various neuropsychiatric symptoms; irregularities in the hypothalamic-pituitary- adrenal (HPA) axis and the hypothalamic-pituitary-thyroid (HPT) axis have been shown in patients with primary depression.

HPT and HPA axes abnormalities observed in patients with depression (Musselman DL, Nemeroff CB. 1996)
HPT axes irregularities: • alterations in thyroid-stimulating hormone (TSH) response to thyrotropin-releasing hormone (TRH) • an abnormally high rate of antithyroid antibodies • elevated cerebrospinal fluid (CSF) TRH concentrations. **HPA axes irregularities:** • adrenocorticoid hypersecretion • enlarged pituitary and adrenal gland size (organomegaly) • elevated corticotropin-releasing factor (CSF) concentrations

Adrenal gland

- Addison's disease: also known as chronic adrenal insufficiency, hypocortisolism, and hypocorticism) is a rare endocrine disorder wherein the adrenal glands, located above the kidneys, produce insufficient steroid hormones (glucocorticoids and often mineralocorticoids). "Addison's disease presenting with psychiatric features in the early stage has the tendency to be overlooked and misdiagnosed."

Thyroid and parathyroid glands



- Graves' disease: an autoimmune disease where the thyroid is overactive, resulting in hyperthyroidism and thyrotoxicosis.
- Hashimoto's thyroiditis: also known chronic lymphocytic thyroiditis is an autoimmune disease in which the thyroid gland is gradually destroyed by a variety of cell and antibody mediated immune processes. Hashimoto's thyroiditis is associated with thyroid peroxidase and thyroglobulin autoantibodies
- Hypothyroidism
- Hyperthyroidism
- Hypoparathyroidism; can affect calcium homeostasis, supplementation of which has completely resolved cases of depression in which hypoparathyroidism is the sole causative factor.

Pituitary tumors

Tumors of the pituitary gland are fairly common in the general population with estimates ranging as high as 25%. Most tumors are considered to be benign and are often an incidental finding discovered during autopsy or as of neuroimaging in which case they are dubbed "incidentalomas". Even in benign cases, pituitary tumors can affect cognitive, behavioral and emotional changes. Pituitary microadenomas are smaller than 10 mm in diameter and are generally considered benign, yet the presence of a microadenoma has been positively identified as a risk factor for suicide.

"... patients with pituitary disease were diagnosed and treated for depression and showed little response to the treatment for depression".

Pancreas

- Hypoglycemia: an overproduction of insulin causes reduced blood levels of glucose. In one study of patients recovering from acute lung injury in intensive care, those patients who developed hypoglycemia while hospitalized showed an increased rate of depression.

Neurological

In addition to pituitary tumors, tumors in various locations in the central nervous system may cause depressive symptoms and be misdiagnosed as depression.

Post concussion syndrome

Post-concussion syndrome (PCS), is a set of symptoms that a person may experience for weeks, months, or occasionally years after a concussion with a prevalence rate of 38–80% in mild traumatic brain injuries, it may also occur in moderate and severe cases of traumatic brain injury. A diagnosis may be made when symptoms resulting from concussion, depending on criteria, last for more than three to six months after the injury, in which case it is termed persistent postconcussive syndrome (PPCS). In a study of the prevalence of post concussion syndrome symptoms in patients with depression utilizing the British Columbia Postconcussion Symptom Inventory: "Approximately 9 out of 10 patients with depression met liberal self-report criteria for a postconcussion syndrome and more than 5 out of 10 met conservative criteria for the diagnosis." These self reported rates were significantly higher than those obtained in a scheduled clinical interview. Normal controls have exhibited symptoms of PCS as well as those seeking psychological services. There is considerable debate over the diagnosis of PCS in part because of the medico-legal and thus monetary ramifications of receiving the diagnosis.

Pseudobulbar affect

Characteristic	PBA	Depression
Duration	Seconds to minutes	Weeks to months
Voluntary control	None to minimal	Can be modulated by the situation
Affect	Unrelated to or independent of mood	Sad, worried, guilty, depressed; most often congruent with mood
Behavior	Does not change	Fatigued, apathetic, occasionally agitated
Perception	No misperceptions	Distorted and negative view of self, others, and future
Insight	Usually not impaired	May be impaired
Stimulus	Nonspecific, minimal or inappropriate to situation	Specific mood-related situations

Adapted from Cummings, 2007.

Diagnostic differences between PBA and depression

Pseudobulbar affect (PBA) is an affective disinhibition syndrome that is largely unrecognized in clinical settings and thus often untreated due to ignorance of the clinical manifestations of the disorder; it may be misdiagnosed as depression. It often occurs

secondary to various neurodegenerative diseases such as amyotrophic lateral sclerosis, and also can result from head trauma. PBA is characterized by involuntary and inappropriate outbursts of laughter and/or crying. PBA has a high prevalence rate with estimates of 1.5 - 2 million cases in the United States alone.

Neurotoxicity

Various compounds have been shown to have neurotoxic effects many of which have been implicated as having a causal relationship in the development of depression.

Cigarette smoking

There has been research which suggests a correlation between cigarette smoking and depression. The results of one recent study suggest that smoking cigarettes may have a direct causal effect on the development of depression. There have been various studies done showing a positive link between smoking, suicidal ideation and suicide attempts.

In a study conducted among nurses, those smoking between 1-24 cigarettes per day had twice the suicide risk; 25 cigarettes or more, 4 times the suicide risk, than those who had never smoked. In a study of 300,000 male U.S. Army soldiers, a definitive link between suicide and smoking was observed with those smoking over a pack a day having twice the suicide rate of non-smokers.

Link Between Smoking Depression and Suicide
"Current daily smoking, but not past smoking, predicted the subsequent occurrence of suicidal thoughts or attempt." "It would seem unwise, nevertheless, to rule out the possibility that smoking might be among the antecedent factors associated with the development of depression." "Abstinence from cigarettes for prolonged periods may be associated with a decrease in depressive symptomatology." "The stress induction model of smoking suggests, however, that smoking causes stress and concomitant negative affect."

Medication

Various medications have been suspected of a having a causal relation in the development of depression; this has been classified as "organic mood syndrome". Some classes of medication such as those used to treat hypertension, have been recognized for decades as having a definitive relationship with the development of depression.

Monitoring of those taking medications which have shown a relationship with depression is often indicated, as well as the necessity of factoring in the use of such medications in the diagnostic process.

- Topical Tretinoin (Retin-A); derived from Vitamin A and used for various medical conditions such as in topical solutions used to treat acne vulgaris. Although applied externally to the skin, it may enter the bloodstream and cross the blood brain barrier where it may have neurotoxic effects.

- Interferons; proteins produced by the human body, three types have been identified *alpha, beta* and *gamma*. Synthetic versions are utilized in various medications used to treat different medical conditions such as the use of interferon-alpha in cancer treatment and hepatitis C treatment. All three classes of interferons may cause depression and suicidal ideation.

Chronic Exposure to Organophosphates

The neurophsychiatric effects of chronic organophosphate exposure include mood disorders, suicidal thinking and behaviour, cognitive impairment and chronic fatigue.

Neuropsychiatric

Bipolar disorder

- Bipolar disorder is frequently misdiagnosed as major depression, and is thus treated with antidepressants alone which is not only not efficacious it is often contraindicated as it may exacerbate hypomania, mania, or cycling between moods. J Clin Psychiatry. 2005 Nov;66(11):1432-40.

  "Misdiagnosed bipolar patients received inappropriate and costly treatment regimens involving overuse of antidepressants and underuse of potentially effective medications. ... It is recommended that steps be taken to minimize misdiagnosis in clinical settings."

Nutritional deficiencies

Nutrition plays a key role in every facet of maintaining proper physical and psychological wellbeing. Insufficient or inadeqaute nutrition can have a profound effect on mental health. The emerging field of Nutritional Neuroscience explores the various connections between diet, neurological functioning and mental health.

- Vitamin B_6:pyridoxal phosphate (PLP) the active form of B_6 is a cofactor in the dopamine serotonin pathway, a deficiency in Vitamin B_6 may cause depressive symptoms.
- Folate (vitamin B_9) - Vitamin B_{12} cobalamin : Low blood plasma and particularly red cell folate and diminished levels of Vitamin B_{12} have been found in patients with depressive disorders. "[W]e suggest that oral doses of both folic acid (800 µg/(mcg) daily) and vitamin B12 (1 mg daily) should be tried to improve treatment outcome in depression."

- Long chain fatty acids: higher levels of omega-6 and lower levels of omega-3 fatty acids has been associated with depression and behavioral change.

Sleep disorders

- Insomnia: While the inability to fall asleep is often a symptom of depression, it can also in some instances serve as the trigger for developing a depressive disorder. It can be transient, acute or chronic. It can be a primary disorder or a co-morbid one.
- Restless legs syndrome:(RLS), also known as Wittmaack-Ekbom's syndrome, is characterized by an irresistible urge to move one's body to stop uncomfortable or odd sensations. It most commonly affects the legs, but can also affect the arms or torso, and even phantom limbs. Restless Leg syndrome has been associated with Major depressive disorder. "Adjusted odds ratio for diagnosis of major depressive disorder... suggested a strong association between restless legs syndrome and major depressive disorder and/or panic disorder."
- Sleep apnea is a sleep disorder characterized by pauses in breathing during sleep. Each episode, called an apnea, lasts long enough for one or more breaths to be missed; such episodes occur repeatedly throughout the sleep cycle. Undiagnosed sleep apnea may cause or contribute to the severity of depression.
- Circadian rhythm sleep disorders, of which too few clinicians are aware, often go untreated or are treated inappropriately, as when misdiagnosed as either primary insomnia or as a psychiatric condition.

Chapter 4

Postpartum Depression

Postpartum Depression	
ICD-10	F53.0
ICD-9	648.4
DiseasesDB	10921
MedlinePlus	007215
eMedicine	med/3408

Postpartum depression (**PPD**), also called **postnatal depression**, is a form of clinical depression which can affect women, and less frequently men, after childbirth. Studies report prevalence rates among women from 5% to 25%, but methodological differences among the studies make the actual prevalence rate unclear. Among men, in particular new fathers, the incidence of postpartum depression has been estimated to be between 1.2% and 25.5%. Postpartum depression occurs in women after they have carried a child, usually in the first few months, and may last up to several months or even a year. Symptoms include sadness, fatigue, changes in sleeping and eating patterns, reduced libido, crying episodes, anxiety, and irritability. It is sometimes assumed that postpartum depression is caused by a lack of vitamins, but studies tend to show that more likely causes are the significant changes in a woman's hormones during pregnancy. On the other hand, others have suggested there is no known correlation between hormones and postpartum mood disorders, and hormonal treatment has not helped postpartum depression victims. Many women recover because of a support group or counseling.

Postpartum Exhaustion (PPE)

PPE is caused by sleep deprivation coupled with hormonal changes in a woman's body shortly after giving birth. It may be mild or severe. Most cases are noted in women who have babies with severe colic or other underlying causes that result in abnormal sleep schedules. PPE is not the same as postpartum depression, but can be classified as a postpartum depression even though exhaustion is usually only caused from extreme fatigue. Medical treatment is minimal. PPE can last from 1 to 20 days and responds with adequate amounts of sleep.

PPD and the "baby blues"

Baby or maternity blues are a mild and transitory moodiness suffered by up to 80% of postnatal women (and in some cases fathers). Symptoms typically last from a few hours to several days, and include tearfulness, irritability, hypochondriasis, sleeplessness, impairment of concentration, feelings of isolation and headache. The maternity blues *are not* the same thing as postpartum depression, nor are they a precursor to postpartum depression or postnatal psychosis.

Symptoms

Symptoms of PPD can occur anytime in the first year postpartum and include, but are not limited to, the following:

- Sadness
- Hopelessness
- Low self-esteem
- Guilt
- A feeling of being overwhelmed
- Sleep and eating disturbances
- Inability to be comforted
- Exhaustion
- Emptiness
- Anhedonia
- Social withdrawal
- Low or no energy
- Becoming easily frustrated
- Feeling inadequate in taking care of the baby
- Impaired speech and writing
- Spells of anger towards others
- Increased anxiety or panic attacks
- Decreased sex drive

One method of detecting Postnatal Depression (PND) is the use of Edinburgh Postnatal Depression Scale. If the new mother scores more than 13, she is likely to develop PND.

Risk factors

While not all causes of PPD are known, a number of factors have been identified as predictors of PPD (the effect size is given in parentheses, where larger values indicate larger effects):

- Formula feeding rather than breast feeding (2.04)
- A history of depression (1.87) (.38 to.39) Beck (2001)
- Cigarette smoking (1.58)
- Low self esteem (.45 to. 47) Beck (2001)

- Childcare stress (.45 to .46) Beck (2001)
- Prenatal depression during pregnancy (.44 to .46) Beck (2001)
- Prenatal anxiety (.41 to .45) Beck (2001)
- Life stress (.38 to .40) Beck (2001)
- Low social support (.36 to .41) Beck (2001)
- Poor marital relationship (.38 to .39) Beck (2001)
- Infant temperament problems/colic (.33 to .34) Beck (2001)
- Maternity blues (.25 to .31) Beck (2001)
- Single parent (.21 to .35) Beck (2001)
- Low socioeconomic status (.19 to .22) Beck (2001)
- Unplanned/unwanted pregnancy (.14 to .17) Beck (2001)

Of these, three factors - formula feeding, a history of depression, and cigarette smoking - have been shown to be additive effects.

These factors are known to correlate with PPD. "Correlation" in this case means that, for example, high levels of prenatal depression are associated with high levels of postnatal depression, and low levels of prenatal depression are associated with low levels of postnatal depression. But this does not mean the prenatal depression causes postnatal depression—they might both be caused by some third factor. In contrast, some factors, such as lack of social support, almost certainly *cause* postpartum depression. (The *causal* role of lack of social support in PPD is strongly suggested by several studies, including O'Hara 1985, Field et al. 1985; and Gotlib et al. 1991.) Anthropologists Kruckman and Stern tested the idea cross culturally, and their pioneering study determined six ways in which postpartum rituals, including the use of the postpartum ritual, la cuarentena, in Chicago Latina mothers, to protect or cushion the expression of mood disorders.

In addition to Beck's meta-analysis cited above, other academic studies have shown a correlation between a mother's race, social class and/or sexual orientation and postpartum depression. In 2006 Segre et al., conducted a study "on the extent to which race/ethnicity is a risk factor" for PPD. Studying 26,877 postpartum women they found that 15.7% were depressed. Of the women suffering from PPD, 25.2% were African American, 22.9% were American Indian/Native Alaskan, 15.5% were White, 15.3% were Hispanic, and 11.5% were Asian/Pacific Islander. Even when "important social factors such as age, income, education, marital status, and baby's health were controlled, African American women still emerged with significantly increased risk for…PPD".

Segre et al., also found a correlation between a mother's social class and PPD. Not surprisingly, women with fewer resources indicate a higher level of postpartum depression and stress than those with more financial resources. Rates of PPD decreased as income increased as follows:

Income	PPD rate
<$10,000	24.3%
$10,000-$19,000	20.0%
$20,000-$29,000	18.8%
$30,000-$39,000	15.3%
$40,000-$49,000	13.7%
$50,000+	10.8%

Likewise, a study conducted by Howell et al. in 2006 confirms Segre's findings that women who are nonwhite and in lower socioeconomic categories have more symptoms of PPD.

In a 2007 study conducted by Ross et al., lesbian and bisexual mothers were tested for PPD and then compared with a heterosexual sample. Ross et al. found that "lesbian and bisexual biological mothers had significantly higher Edinburgh Postnatal Depression Scale (EPDS) scores than the…sample of heterosexual women." The Ross study suggests that PPD may be more common among lesbian and bisexual mothers. From a study conducted in 2005 by Ross, the higher rates of PPD in lesbian/bisexual mothers than heterosexual mothers may be due to less "social support, particularly from their families of origin and…additional stress due to homophobic discrimination" in society.

Although profound hormonal changes after childbirth are often claimed to cause PPD, there is little evidence that variation in pregnancy hormone levels is correlated with variation in PPD levels: Studies that have examined pregnancy hormone levels and PPD have usually failed to find a relationship. Further, fathers, who are not undergoing profound hormonal changes, suffer PPD at relatively high rates (e.g., Goodman 2004). Finally, all mothers experience these hormonal changes, yet only about 10–15% suffer PPD. This does *not* mean, however, that hormones do not play a role in PPD. For example, *in women with a history of PPD*, a hormone treatment simulating pregnancy and parturition caused these women to suffer mood symptoms. The same treatment, however, did not cause mood symptoms in women with no history of PPD. One interpretation of these results is that there is a subgroup of women who are vulnerable to hormone changes during pregnancy. Another interpretation is that simulating a pregnancy will trigger PPD in women who are vulnerable to PPD for any of the reasons indicated by Beck's meta-analysis (summarized above).

Profound lifestyle changes brought about by caring for the infant are also frequently claimed to cause PPD, but, again, there is little evidence for this hypothesis. Mothers who have had several previous children without suffering PPD can nonetheless suffer it with their latest child (Nielsen Forman et al. 2000). Plus, most women experience profound lifestyle changes with their first pregnancy, yet most do not suffer PPD.

Sometimes a pre-existing mental illness can be brought to the forefront through PPD. It is widely found in women whose families have a history of mental illnesses and disorders

such as bipolar disorder, schizophrenia and autism, and above-average rates of drug addiction and alcoholism.

In 2009, researchers at the University of California, Irvine, reported that the levels of placental corticotropin-releasing hormone (CRH) during the 25th week of pregnancy may help predict a woman's chances of developing postpartum depression.

Evolutionary psychological hypothesis

Human infants require an extraordinary degree of care. Lack of support from fathers and/or other family member will increase the costs borne by mothers, whereas infant health problems will reduce the evolutionary benefits to be gained (Hagen 1999). If ancestral mothers did not receive enough support from fathers or other family members, they may not have been able to afford raising the new infant without harming any existing children, or damaging their own health (nursing depletes mothers' nutritional stores, placing the health of poorly nourished women in jeopardy).

For mothers suffering inadequate social support or other costly and stressful circumstances, negative emotions directed towards a new infant could serve an important evolved function by causing the mother to reduce her investment in an unaffordable infant, thereby reducing her costs. Numerous studies support the correlation between postpartum depression and lack of social support or other childcare stressors (Beck 2001; Hagen 1999).

Kruckman, using observations from anthropological field work, suggests that supportive rituals and knowledge, if projected to the mother in a meaningful and sincere fashion, can affect the hypothalamus, pituitary and adrenal function and the production of endocrine signal molecules, and reduce the expression of anxiety or panic in postpartum women.

Mothers with postpartum depression can unconsciously exhibit fewer positive emotions and more negative emotions toward their children, are less responsive and less sensitive to infant cues, less emotionally available, have a less successful maternal role attainment, and have infants that are less securely attached; and in more extreme cases, some women may have thoughts of harming their children (Beck 1995, 1996b; Cohn et al. 1990, 1991; Field et al. 1985; Fowles 1996; Hoffman and Drotar 1991; Jennings et al. 1999; Murray 1991; Murray and Cooper 1996). In other words, most mothers with PPD are suffering some kind of cost, like inadequate social support, and consequently are mothering less.

In this view, mothers with PPD do not have a *mental illness*, but instead cannot afford to take care of the new infant without more social support, more resources, etc. Treatment should therefore focus on helping mothers get what they need.

Effects on the parent-infant relationship

Postpartum depression may lead mothers to be inconsistent with childcare. Women diagnosed with postpartum depression often focus more on the negative events of childcare, resulting in poor coping strategies (Murray).

There are four groups of coping methods, each divided into a different style of coping subgroups. Avoidance coping is one of the most common strategies used (Murray). It consists of denial and behavioral disengagement subgroups (for example, an avoidant mother might not respond to her baby crying). This strategy however, does not resolve any problems and ends up negatively impacting the mother's mood, similarly of the other coping strategies used (Honey).

Four coping strategies:

- ***Avoidance coping:*** denial, behavioral disengagement
- ***Problem-focused coping:*** active coping, planning, positive reframing
- ***Support seeking coping:*** emotional support, instrumental support
- ***Venting coping:*** venting, self-blame

Security

Mothers who resort to avoidance coping and so don't respond to their infants' needs may make the infant feel insecure {}. According to Edhborg's article on long-term impacts, insecurity can lead to infant stress and infant avoidance, where the infant may become so subdued that it will not interact with the mother or any other adult. This is a concern because months two through six in an infant's life are very important; it is in these months that the infant develops some interaction and cognitive skills. Parent-infant interaction is most essential during this time because it builds the connection not only with the mother, but others as well. It is also the time of most risk for the child because of a possible increased onset of depression in the mother (Long-term). The lack of interaction can lead to difficulties in parent-infant communication and result in poorer infant performance (Murray). Multiple factors must be considered when evaluating the capacity of a seriously depressed mother to provide a safe-enough caregiving environment that can support the healthy development of her baby and her relationship with that baby. Such factors, including maternal attachment history, present social supports, insight, and ability to accept help are often best considered by an indisciplinary professional treatment team that includes infant mental health specialists or other mental health practitioners with experience in working with children and families.

Attachment study

A study by Edhborg on mother-child attachment looked at 45 randomly selected mother-child pairs. These pairs were chosen using the Edinburgh Postnatal Depression Scale (EPDS) form, measuring postpartum depression in the community. 326 women returned the form and of the 326, 24 scoring above twelve were recruited and 21 women scoring

less than nine were recruited. A score above twelve is considered "potentially depressed" and a score of less than nine is considered to have no form of depression. The 45 mother-child pairs were videotaped, in their homes, for five minutes in three different situations. Mother and child were first put in a room with a standard set of toys, to represent a control play. In the second situation, mother and child were allowed to play freely in an average toy room. In the third situation, the mother was asked to leave the room as if she had to check on something, like she would regularly do in their home environment, and then return.

Senior Psychologists then scored the interaction between mother and child. The first two taped situations were scored on a five point scale; 1 (being the area of most concern) to 5 (being an area of strength). In the third situation, the attachment behavior was put into three groups based on how the child reacted to the mother's return.

Three classified groups:

- ***Secure and joyful attachment***: consists of child greeting mother with joy and being comforted by her presence.
- ***Secure attachment but restricted in expressed enjoyment and pleasure***: consists of the child acknowledging the mother, but showing less joy than would normally be expected.
- ***Insecure attachment***: consists of child showing signs of avoidance and resistance. In the form of resistance the child would go to the mother, but then pull away and often repeat this action.

Analysis showed only one difference between the groups. In the free play situation, children of mothers with high EPDS scores showed less interest in playing with their mothers and exploring on their own, than the children of mothers with low EPDS scores. The mothers too only showed one difference. Those with a high EDPS score showed little maternal emotional availability to the child. Following the results, Edhborg performed a cluster analysis, keeping interest on the different interaction styles. Some children did show signs of depression, but when comparing the children it was found that there is no significance with the EPDS scores and the interaction styles. The study did find, however, that children of high EPDS scorers were less involved in the free play situation than the children of low EPDS scorers, showing that children of high EPDS are more likely to be insecure. When performing the structured task from the first situation it showed that the mothers with high EPDS were “aware of their unavailability for the child in the early postpartum period and thus tried harder… to help their children succeed in the task” (Edhborg). This overreaction proves that too much interaction can cause a negative mood in the child and a continuing difficulty in mother-child communication. Attachment issues have been shown to be a problem in older children, also. As a result of being exposed to the depression symptoms, as an infant, older children may have impaired cognitive and socio-emotional developments. The lack of attachment can also cause troubles in the interaction with others and personal independence (Long-term). Children with these issues have a higher risk of being diagnosed with depression later in life as well (Honey). John Bowlby's attachment theory explains how infants learn about

their environment while keeping their caregiver close. Bowlby explains his theories with the principles of variety, heredity, and natural selection. Children need balance between the outside world and the love and support of their parents. Bowlby concentrates on a child's instinct and human nature, in opposition of Locke who believes that a newborn has no instinct to direct him or her. (Chasse, J.)

Prevention

Early identification and intervention improves long term prognoses for most women. Some success with preemptive treatment has been found as well. A major part of prevention is being informed about the risk factors, and the medical community can play a key role in identifying and treating postpartum depression. Women should be screened by their physician to determine their risk for acquiring postpartum depression. Currently, Alberta is the only province in Canada with universal PPD screening which has been in place since 2003. The PPD screening is carried out by Public Health nurses in conjunction with the baby's immunization schedule. Also, proper exercise and nutrition appears to play a role in preventing postpartum, and general, depression.

Nutrition

Pregnant, nursing and postpartum women are strongly encouraged to seek the medical advice of their obstetrician, primary care physician, registered dietitian, or midwife regarding optimal nutrition during pregnancy and after birth.

The following nutritional information may be beneficial in achieving a well-balanced diet during and after pregnancy, but studies are needed to confirm their role in preventing postpartum depression.

Omega-3 fatty acids: Some experts believe that postpartum depression can be attributed to depletion of omega 3 fatty acids from the mother's brain to support development of the brain of the fetus or breast fed infant. This can be prevented by ensuring that sufficient omega 3 fatty acids are provided in the mother's diet. Good natural sources of omega 3 fatty acids include edible linseed oil, certain fish, grass fed rather than grain fed meat, and eggs from chickens fed on flax seed or other feed high in omega 3 fats. Omega 3 fatty acids can also be purchased in capsule form as a dietary supplement.

Protein can be found in a wide variety of foods. Some examples follow: 3 ounces of most meat products contain 25 grams of protein, 3 large eggs have approximately 19 grams, and 3 ounces of Swiss cheese have about 15 grams.

Hydration: One of the most important roles in any diet (especially for pregnant and nursing mothers) is that of hydration. Physicians may recommend that pregnant women consume ten 8-ounce glasses of water every day. Mothers who are nursing are strongly urged to drink a tall glass of water, milk or juice before sitting down to breastfeed their child. Women should consult with their physicians about caffeine and alcohol consumption postpartum.

Vitamins: A pregnant and postpartum woman should speak with her physician for information about, and a recommendation for, a daily prenatal/postnatal vitamin supplement.

B Vitamins Some limited research has indicated that the intake of B vitamins, specifically riboflavin, can help reduce the chance of post partum depression. B vitamins are water soluble and must be replenished each day.

Appetite: If a woman finds herself with a loss of appetite or other eating disturbance, she should consult her physician. This may be a sign of postpartum depression and therefore should be discussed with a doctor.

Treatment

Numerous scientific studies and scholarly journal articles support the notion that postpartum depression is treatable using a variety of methods. If the cause of PPD can be identified, as described above under "social risk factors," treatment should be aimed at mitigating the root cause of the problem, including increased partner support, additional help with childcare, cognitive therapy, etc.

Women need to be taken seriously when symptoms occur. This is a twofold practice: First, the postpartum woman will want to trust her intuition about how she is feeling and believe that her symptoms are real enough to tell her significant other, a close friend, and/or her medical practitioner; erring on the side of caution will go a long way in the treatment of PPD. Second, the people in whom she confides must take her symptoms seriously as well, aiding her with treatment and support. Partners, friends and physicians may notice changes in a postpartum mother that she may not. Knowing that PPD is treatable with a variety of methods can make persistence in seeking treatment easier.

Various treatment options include:

- Medical evaluation to rule out physiological problems
- Cognitive behavioral therapy (a form of psychotherapy)
- Possible medication
- Support groups
- Home visits/Home visitors
- Healthy diet
- Consistent/healthy sleep patterns

An experienced medical professional will work *with* a postpartum mother to develop a treatment plan that is right for her. This plan may include any combination of the above options, and might include some discussion or feedback from/with a partner. If a woman suffering from PPD does not feel she is being taken seriously or is being recommended a treatment plan she does not feel comfortable with, she will want to seek a second opinion.

A 1997 study conducted by Appleby *et al.*, confirms that postpartum depressed mothers' symptoms promptly improved at similar rates when treated with cognitive behavioral therapy or the antidepressant fluoxetine. "A group of 61 depressed mothers completed a 12-week treatment program with or without the antidepressant plus one session versus six sessions of counseling." Improvement followed after "one to four weeks of either treatment." The findings of Appleby et al.'s study conclusively showed that combining counseling with drug therapy *did not* add to the improvement of just drug therapy or just counseling. This suggests that counseling is equally as effective a treatment for PPD as medication, and that "the choice of treatment [psychotherapy vs. medication] may…be made by the women themselves". Other forms of therapy (like group therapy and home visitors) are also effective treatments for PPD.

A woman will want to discuss the various treatment options available with her physician and, if considering drug therapy, should speak about which medications are safe to take while breastfeeding.

Treatment for PPD can reduce the length of suffering and its severity. Untreated, the Baby Blues may go away on its own (and does in most cases). PPD may or may not go away without treatment. Speaking to a health care provider as soon as symptoms occur is the safest way to ensure prompt treatment and return to normal life.

According to The National Institutes of Mental Health, studies show that the childbearing years are when a woman is most likely to experience depression in her lifetime. Approximately 15% of all women will experience postpartum depression following the birth of a child. (Chasse, J). When the mental health of the mother is compromised, it affects the entire family.

Psychosis

Postpartum psychosis is a separate mental illness, which involves a complete break with reality. Although sometimes confused with or erroneously referred to as postpartum depression, postpartum psychosis is a very different disorder. It is less common than PPD, and it involves the onset of psychotic symptoms that may include thought disturbances, delusions, hallucinations and/or disorganized speech or behavior.

Treatment for Postnatal Psychosis is essential; it will not go away without medical attention.

Chapter 5

Seasonal Affective Disorder

Seasonal affective disorder (**SAD**), also known as **winter depression** or **winter blues**, is a mood disorder in which people who have normal mental health throughout most of the year experience depressive symptoms in the winter, or, less frequently, in the summer, spring or autumn, repeatedly, year after year. In the Diagnostic and Statistical Manual of Mental Disorders (DSM-IV), SAD is not a unique mood disorder, but is "a specifier of major depression".

Once regarded skeptically by the experts, seasonal affective disorder is now well established. Epidemiological studies estimate that its prevalence in the adult population of the US ranges from 1.4 percent (Florida) to 9.7 percent (New Hampshire).

The US National Library of Medicine notes that "some people experience a serious mood change when the seasons change. They may sleep too much, have little energy, and may also feel depressed. Though symptoms can be severe, they usually clear up." The condition in the summer is often referred to as reverse seasonal affective disorder, and can also include heightened anxiety.

SAD was first formally described and named in 1984 by Norman E. Rosenthal and colleagues at the National Institute of Mental Health.

There are many different treatments for classic (winter-based) seasonal affective disorder, including light therapy with sunlight or bright lights, antidepressant medication, cognitive-behavioral therapy, ionized-air administration, and carefully timed supplementation of the hormone melatonin.

Symptoms

Symptoms of SAD may consist of difficulty waking up in the morning, morning sickness, tendency to oversleep as well as to overeat, and especially a craving for carbohydrates, which leads to weight gain. Other symptoms include a lack of energy, difficulty concentrating on completing tasks, and withdrawal from friends, family, and social activities. All of this leads to the depression, pessimistic feelings of hopelessness, and lack of pleasure which characterize a person suffering from this disorder.

People who experience summer SAD (spring and summer depression) show symptoms of classic depression including insomnia, anxiety, irritability, decreased appetite, weight loss, social withdrawal, and a decreased sex drive. Additionally, many patients are unable to cope with the increased temperatures during spring and summer.

Diagnostic criteria

According to the American Psychiatric Association DSM-IV criteria, Seasonal Affective Disorder is not regarded as a separate disorder. It is called a "course specifier" and may be applied as an added description to the pattern of major depressive episodes in patients with major depressive disorder or patients with bipolar disorder.

The "Seasonal Pattern Specifier" must meet four criteria: depressive episodes at a particular time of the year; remissions or mania/hypomania at a characteristic time of year; these patterns must have lasted two years with no nonseasonal major depressive episodes during that same period; and these seasonal depressive episodes outnumber other depressive episodes throughout the patient's lifetime. The Mayo Clinic describes three types of SAD, each with its own set of symptoms.

In the popular culture, sometimes the term "seasonal affective disorder" is applied inaccurately to the normal shift to lower energy levels in winter, leading people to believe they have a physical problem that should be addressed with various therapies or drugs.

Physiology

Seasonal mood variations are believed to be related to light. An argument for this view is the effectiveness of bright-light therapy. SAD is measurably present at latitudes in the Arctic region, such as Finland (64º 00´N) where the rate of SAD is 9.5%. Cloud cover may contribute to the negative effects of SAD.

The symptoms of SAD mimic those of dysthymia or even major depressive disorder. There is also potential risk of suicide in some patients experiencing SAD. One study reports 6-35% of sufferers required hospitalization during one period of illness. At times, patients may not feel depressed, but rather lack energy to perform everyday activities.

Various proximate causes have been proposed. One possibility is that SAD is related to a lack of serotonin, and serotonin polymorphisms could play a role in SAD, although this has been disputed. Mice incapable of turning serotonin into N-acetylserotonin (by Serotonin N-acetyltransferase) appear to express "depression-like" behavior, and antidepressants such as fluoxetine increase the amount of the enzyme Serotonin N-acetyltransferase, resulting in an antidepressant-like effect. Another theory is that the cause may be related to melatonin which is produced in dim light and darkness by the pineal gland, since there are direct connections, via the retinohypothalamic tract and the suprachiasmatic nucleus, between the retina and the pineal gland.

Subsyndromal Seasonal Affective Disorder is a milder form of SAD experienced by an estimated 14.3% (vs. 6.1% SAD) of the U.S. population. The blue feeling experienced by both SAD and SSAD sufferers can usually be dampened or extinguished by exercise and increased outdoor activity, particularly on sunny days, resulting in increased solar exposure. Connections between human mood, as well as energy levels, and the seasons are well documented, even in healthy individuals.

Mutation of a gene expressing melanopsin has been implicated in the risk of having Seasonal Affective Disorder.

History

SAD was first systematically reported and named in the early 1980s by Norman E. Rosenthal, M.D., and his associates at the National Institute of Mental Health (NIMH). Rosenthal was initially motivated by his desire to discover the cause of his own experience of depression during the dark days of the northern US winter. He theorized that the lesser amount of light in winter was the cause. Rosenthal and his colleagues then documented the phenomenon of SAD in a placebo-controlled study utilizing light therapy. A paper based on this research was published in 1984. Although Rosenthal's ideas were initially greeted with skepticism, SAD has become well recognized, and his 1993 book, *Winter Blues* has become the standard introduction to the subject.

Research on SAD in the United States began in 1970 when Herb Kern, a research engineer, had also noticed that he felt depressed during the winter months. Kern suspected that scarcer light in winter was the cause and discussed the idea with scientists at the NIMH who were working on bodily rhythms. They were intrigued, and responded by devising a lightbox to treat Kern’s depression. Kern felt much better within a few days of treatments, as did other patients treated in the same way.

Origin

In many species, activity is diminished during the winter months in response to the reduction in available food and the difficulties of surviving in cold weather. Hibernation is an extreme example, but even species that do not hibernate often exhibit changes in behavior during the winter. It has been argued that SAD is an evolved adaptation in humans that is a variant or remnant of a hibernation response in some remote ancestor. Presumably, food was scarce during most of human prehistory, and a tendency toward low mood during the winter months would have been adaptive by reducing the need for calorie intake. The preponderance of women with SAD suggests that the response may also somehow regulate reproduction.

Treatment

One type of light therapy lamp

There are many different treatments for classic (winter-based) seasonal affective disorder, including light therapy, medication, ionized-air administration, cognitive-behavioral therapy and carefully timed supplementation of the hormone melatonin.

Photoperiod-related alterations of the duration of melatonin secretion may affect the seasonal mood cycles of SAD. This suggests that light therapy may be an effective treatment for SAD. Light therapy uses a lightbox which emits far more lumens than a customary incandescent lamp. Bright white "full spectrum" light at 10,000 lux, blue light at a wavelength of 480 nm at 2,500 lux or green light at a wavelength of 500 nm at 350 lux are used, with the first-mentioned historically preferred.

Bright light therapy is effective with the patient sitting a prescribed distance, commonly 30–60 cm, in front of the box with her/his eyes open but not staring at the light source for 30–60 minutes. A 1995 study showed that green light therapy at doses of 350 lux produces melatonin suppression and phase shifts equivalent to 10,000 lux bright light therapy in winter depressives. A study published in May 2010 suggests that the blue light often used for SAD treatment should perhaps be replaced by green or white illumination. Discovering the best schedule is essential. One study has shown that up to 69% of

patients find lightbox treatment inconvenient and as many as 19% stop use because of this.

Dawn simulation has also proven to be effective; in some studies, there is an 83% better response when compared to other bright light therapy. When compared in a study to negative air ionization, bright light was shown to be 57% effective vs. dawn simulation 50%. Patients using light therapy can experience improvement during the first week, but increased results are evident when continued throughout several weeks. Most studies have found it effective without use year round but rather as a seasonal treatment lasting for several weeks until frequent light exposure is naturally obtained.

Light therapy can also consist of exposure to sunlight, either by spending more time outside or using a computer-controlled heliostat to reflect sunlight into the windows of a home or office.

SSRI (selective serotonin reuptake inhibitor) antidepressants have proven effective in treating SAD. Bupropion is also effective as a prophylactic. Effective antidepressants are fluoxetine, sertraline, or paroxetine. Both fluoxetine and light therapy are 67% effective in treating SAD according to direct head-to-head trials conducted during the 2006 Can-SAD study. Subjects using the light therapy protocol showed earlier clinical improvement, generally within one week of beginning the clinical treatment.

Negative air ionization, which involves releasing charged particles into the sleep environment, has been found effective with a 47.9% improvement if the negative ions are in sufficient density (quantity). Depending upon the patient, one treatment (e.g., lightbox) may be used in conjunction with another (e.g., medication).

Modafinil may be an effective and well-tolerated treatment in patients with seasonal affective disorder/winter depression.

Alfred J. Lewy of Oregon Health & Science University and others see the cause of SAD as a misalignment of the sleep-wake phase with the body clock, circadian rhythms out of synch, and treat it with melatonin in the afternoon. Correctly timed melatonin administration shifts the rhythms of several hormones en bloc.

Another explanation is that vitamin D levels are too low when people do not get enough Ultraviolet-B on their skin. An alternative to using bright lights is to take vitamin D supplements. However, one study did not show a link between vitamin D levels and depressive symptoms in elderly Chinese.

Incidence

Nordic countries

Winter depression is a common slump in the mood of some inhabitants of most of the Nordic countries. It was first described by the 6th century Goth scholar Jordanes in his

Getica wherein he described the inhabitants of Scandza (Scandinavia). Iceland, however, seems to be an exception. A study of more than 2000 people there found the prevalence of seasonal affective disorder and seasonal changes in anxiety and depression to be unexpectedly *low* in both sexes. The study's authors suggested that propensity for SAD may differ due to some genetic factor within the Icelandic population. A study of Canadians of wholly Icelandic descent also showed low levels of SAD. It has more recently been suggested that this may be attributed to the large amount of fish traditionally eaten by Icelandic people, 225 lb per person per year as opposed to about 50 lb in the US and Canada, rather than to genetics. Fish is high in vitamin D. Fish also contains docosahexaenoic acid (DHA), which has been shown to help with a variety of neurological dysfunctions.

Other countries

In the United States, a diagnosis of seasonal affective disorder was first proposed by Norman E. Rosenthal, MD in 1984. Rosenthal wondered why he became sluggish during the winter after moving from sunny South Africa to New York. He started experimenting increasing exposure to artificial light, and found this made a difference. In Alaska it has been established that there is a SAD rate of 8.9%, and an even greater rate of 24.9% for subsyndromal SAD.

Around 20% of Irish people are affected by SAD, according to a survey conducted in 2007. The survey also shows women are more likely to be affected by SAD than men. An estimated 10% of the population in the Netherlands suffer from SAD.

SAD and bipolar disorder

Most people with SAD experience major depressive disorder, but as many as 20% may have or may go on to develop a bipolar disorder (manic-depressive disorder). It is important to discriminate the improved mood associated with recovery from the winter depression and a manic episode because there are important treatment differences. In these cases, people with SAD may experience depression during the winter and hypomania in the summer.

Chapter 6

Biology of Depression

Scientific studies have found that numerous brain areas show altered activity in depressed patients. It has not been possible to determine a single cause of depression. Research on the brains of depressed patients usually shows disturbed pattern of interaction between multiple parts of the brain. Here are the areas that are most strongly affected:

Raphe nuclei

The raphe nuclei are a group of small nuclei in the upper brain stem, located directly at the midline of the brain. They are the sole source of serotonin in the brain. Despite their small size, they project very widely, and are involved in a very diverse set of functions. Most antidepressants are serotonergic. Serotonin system dysfunction cannot be the sole cause of depression, though: antidepressants usually bring serotonin levels up to normal very quickly, but it often takes at least two to four weeks before mood improves significantly. The 5-HTT gene regulates a chemical called serotonin. Serotonin works as the neurotransmitter and helps with the modulation of things such as anxiety, anger, appetite, sexuality, sleep, mood, and several other things. People with depression often have impaired 5-HTT genes. There are two forms of the 5-HTT gene and everyone has two 5-HTT genes. (Levinson) There is a long form of 5-HTT and a short form of 5-HTT. Research shows that people with both 5-HTT genes being the long form are less likely to become depressed while people with one short and one long or two short forms are more likely to develop depression. Research is still being conducted to find more information. The functions of serotonin are difficult to describe in a simple way. In some circumstances serotonin seems to act as a signal of "repletion" or "satisfaction". Thus, satiation after eating, and orgasm following sex, both produce release of serotonin. In animals that have hierarchical social structures, dominant individuals show higher levels of serotonin metabolites than lower-status individuals. In the brain, serotonin exerts a suppressive effect on both the reward system and punishment system, and therefore is likely to reduce the intensity of motivation whether aversive or appetitive. (One of the most common but least-discussed side effects of antidepressants is to reduce sex drive).

Suprachiasmatic nucleus (SCN)

The suprachiasmatic nucleus (SCN) is the control center for the body's "biological clock". It contains neurons whose activity waxes and wanes throughout the day. The output from the SCN controls the sleep/wake cycle as well as a number of other

biological rhythms, such as fluctuations in body temperature. Disturbances of these cycles are a consistent symptom of depression, especially of the melancholic type. The "classic" pattern is for depressed people to have great difficulty falling asleep at night, and then to wake bolt upright at around 3 AM. The waking is usually preceded by a rise in body temperature, which in non-depressed people does not usually occur until several hours later. It is a common observation that antidepressants produce a return to normal sleep patterns before they produce an improvement in mood: if good sleep does not return, it is a strong sign that the treatment is not going to be effective. Conversely, disruptions to sleep are often the first indication of impending relapse.

There is a powerful interaction between the Raphe nuclei and the SCN. On one hand, the Raphe nuclei send a strong serotonergic projection to the SCN. In animal studies, this input has been shown to modulate the ability of light to reset the timing of the biological clock: the more serotonin, the stronger the effects of light. On the other hand, the biological clock exerts a strong influence on the Raphe nuclei: serotonin levels drop during sleep, and fall almost to nothing during REM (dreaming) sleep. It is worth noting that one of the characteristics of sleep in depressed people is that REM tends to appear very soon after sleep onset, whereas in non-depressed people it does not usually dominate sleep until the last hours, in the early morning. Antidepressants are powerful suppressors of REM.

Hypothalamic-Pituitary-Adrenal (HPA) axis

The Hypothalamic-pituitary-adrenal axis is a chain of structures that are activated during the body's response to stressors of various sorts. It often shows increased activation in depressed people, and drugs that reduce its activity are sometimes effective in reducing symptoms. The HPA influences many parts of the brain, including the Raphe nuclei.

Ventral tegmental area (VTA)

The ventral tegmentum (or ventral tegmental area) is a small area in the basal midbrain which is a critical part of the brain's reward system. It sends projections to the *nucleus accumbens* that use the neurotransmitter dopamine. Addictive drugs universally increase the effects of dopamine in this system, whereas drugs that oppose dopamine produce anhedonia of the sort seen in depressed people. Dopamine-enhancers such as cocaine often relieve the lack-of-pleasure in dopamine, but the effects only last as long as a drug is present in the body: that is, they temporarily alleviate one of the main symptoms, but do not help to cure the disease.

Nucleus accumbens (NAc)

Long-term exposure to various unavoidable stress factors decreases dopamine release in the NAc shell, as it was shown in the forced swimming test, an animal model of depression.

Anterior cingulate cortex (ACC)

The anterior cingulate cortex is activated by negative experiences of many types, and consistently shows higher levels of activity in depressed people than in non-depressed people. The functions of the ACC are controversial, but one proposal is that it mediates the conscious experience of suffering. Several decades ago, trials were made of ablating parts of the ACC in an attempt to relieve intolerable pain in patients who were terminally ill. These patients reported that after the surgery, they could still perceive the physical sensations of pain, but they no longer found them distressing. (The effects of heroin and morphine are sometimes described in the same way.) Very recently, clinical experiments were made in using deep brain stimulation to temporarily inactivate the ACC in severely depressed patients. This was not effective in all cases, but in some patients very striking results were achieved, with a perceptible lifting of mood immediately apparent to the patient as soon as the stimulus was applied.

Subgenual cingulate

Recent studies have shown that Broadmann area 25, also known as Subgenual cingulate is metabolically overactive in treatment-resistant depression. This region is extremely rich in serotonin transporters and is considered as a governor for a vast network involving areas like hypothalamus and brain stem, which influences changes in appetite and sleep; the amygdala and insula, which affect the mood and anxiety; the hippocampus, which plays an important role in memory formation; and some parts of the frontal cortex responsible for self-esteem. Thus disturbances in this area or a smaller than normal size of this area contributes to depression. Deep Brain Stimulations of this area have been successful in reducing its elevated activity and thus curing depression in patients that could not be cured by anti-depressants.

Monoamine hypothesis

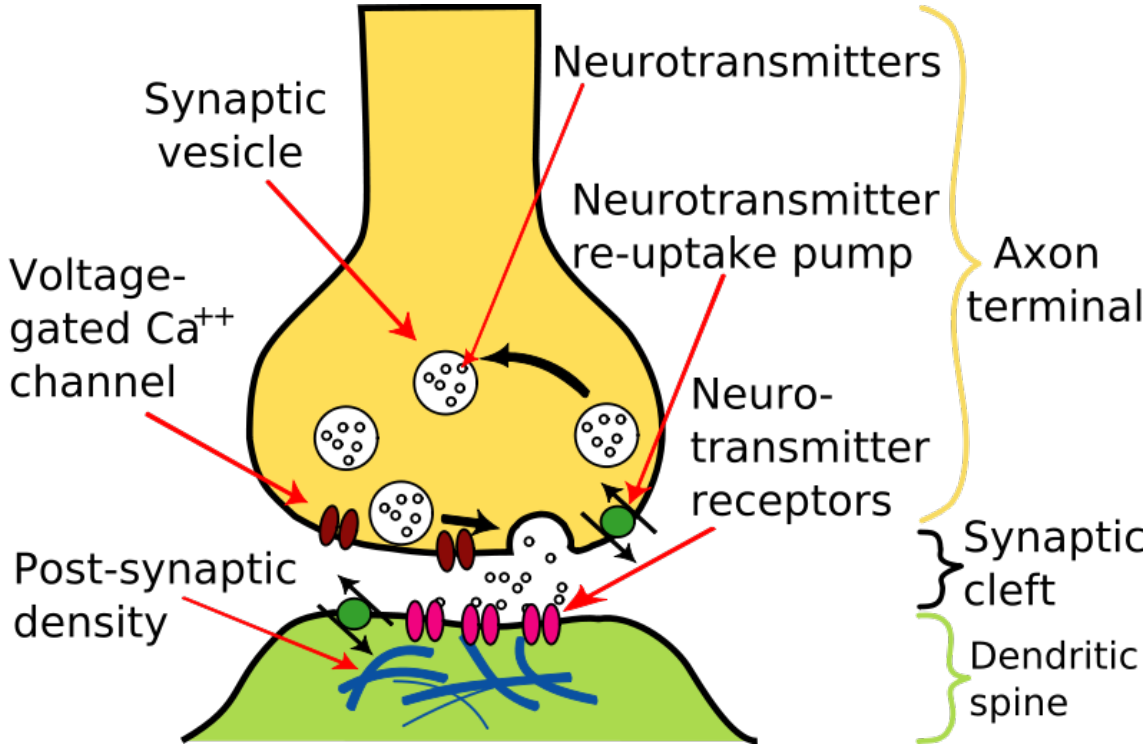
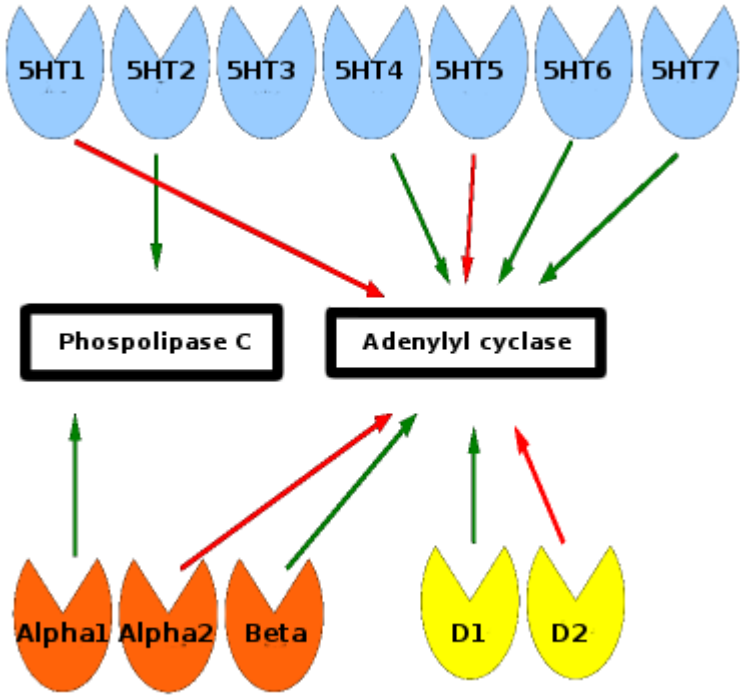


Illustration of the major elements in a prototypical synapse. Synapses are gaps between nerve cells. These cells convert their electrical impulses into bursts of chemical relayers, called neurotransmitters, which travel across the synapses to receptors on adjacent cells, triggering electrical impulses to travel down the latter cells.

Most antidepressants increase synaptic levels of the monoamine neurotransmitter serotonin. They may also enhance the levels of two other neurotransmitters, norepinephrine and dopamine. This observation gave rise to the monoamine hypothesis of depression. In its contemporary formulation, the monoamine hypothesis postulates that the deficit of certain neurotransmitters is responsible for the corresponding features of depression: "Norepinephrine may be related to alertness and energy as well as anxiety, attention, and interest in life; [lack of] serotonin to anxiety, obsessions, and compulsions; and dopamine to attention, motivation, pleasure, and reward, as well as interest in life." The proponents of this hypothesis recommend choosing the antidepressant with the mechanism of action impacting the most prominent symptoms. The anxious and irritable patients should be treated with SSRIs or norepinephrine reuptake inhibitors, and the ones with the loss of energy and enjoyment of life—with norepinephrine and dopamine enhancing drugs.



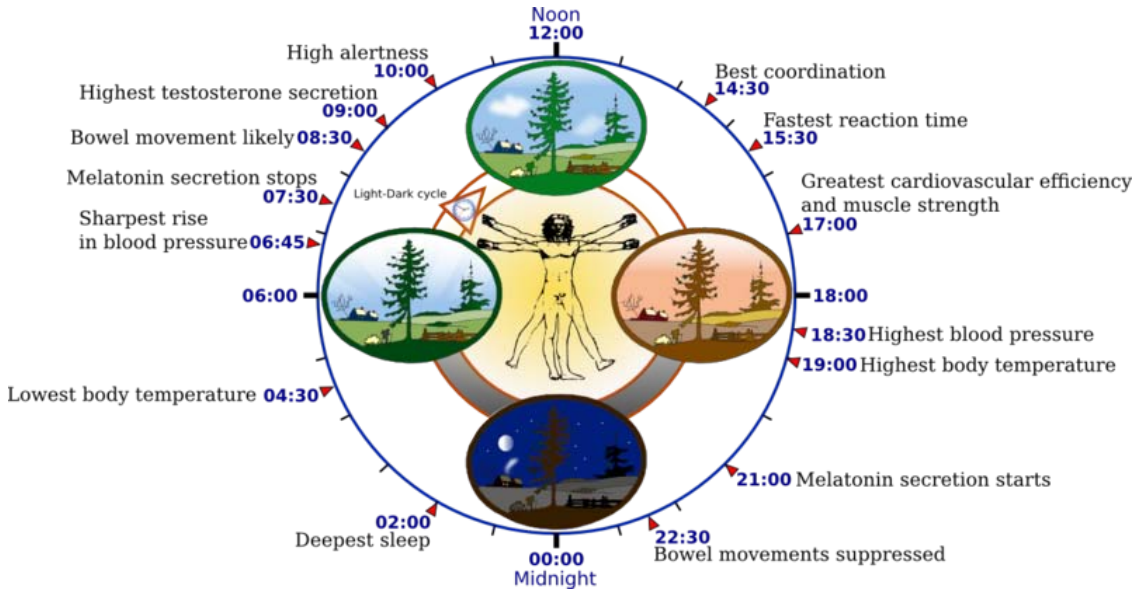
Monoamine receptors affect phospholipase C and adenylyl cyclase inside of the cell. Green arrows means stimulation and red arrows inhibition. Serotonin receptors are blue, norepinephrine orange, and dopamine yellow. Phospolipase C and adenylyl cyclase start a signaling cascade which turn on or off genes in the cell. The 5HT-3 receptor is associated with gastrointestinal adverse effects and has no relationship to the other monoamine receptors.

Consistent with the monoamine hypothesis, a longitudinal study uncovered a moderating effect of the serotonin transporter (5-HTT) gene on stressful life events in predicting depression. Specifically, depression seems especially likely to follow stressful life events, but even more so for people with one or two short alleles of the 5-HTT gene. Serotonin may help to regulate other neurotransmitter systems, and decreased serotonin activity may "permit" these systems to act in unusual and erratic ways. Facets of depression may be emergent properties of this dysregulation.

In the past two decades, research has uncovered multiple limitations of the monoamine hypothesis, and its inadequacy has been criticized within the psychiatric community. Intensive investigation has failed to find convincing evidence of a primary dysfunction of a specific monoamine system in patients with major depressive disorders. The antidepressants that do not act through the monoamine system, such as tianeptine and opipramol, have been known for a long time. Experiments with pharmacological agents that cause depletion of monoamines have shown that this depletion does not cause depression in healthy people nor does it worsen the symptoms in depressed patients. Already limited, the monoamine hypothesis has been further oversimplified when presented to the general public.

An offshoot of the monoamine hypothesis suggests that monoamine oxidase A (MAO-A), an enzyme which metabolizes monoamines, may be overly active in depressed people. This would, in turn, cause the lowered levels of monoamines. This hypothesis received support from a PET study, which found significantly elevated activity of MAO-A in the brain of some depressed people. In genetic studies, the alterations of MAO-A-related genes have not been consistently associated with depression. Contrary to the assumptions of the monoamine hypothesis, lowered but not heightened activity of MAO-A was associated with the depressive symptoms in youth. This association was observed only in maltreated youth, indicating that both biological (MAO genes) and psychological (maltreatment) factors are important in the development of depressive disorders. In addition, some evidence indicates that problems in information processing within neural networks, rather than changes in chemical balance, might underlie depression.

Circadian rhythm



Depression may be related to the same brain mechanisms that control the cycles of sleep and wakefulness.

Depression may be related to abnormalities in the circadian rhythm, or biological clock. For example, rapid eye movement (REM) sleep—the stage in which dreaming occurs—may be quick to arrive and intense in depressed people. REM sleep depends on decreased serotonin levels in the brain stem, and is impaired by compounds, such as antidepressants, that increase serotonergic tone in brain stem structures. Overall, the serotonergic system is least active during sleep and most active during wakefulness. Prolonged wakefulness due to sleep deprivation activates serotonergic neurons, leading to processes similar to the therapeutic effect of antidepressants, such as the selective serotonin reuptake inhibitors (SSRIs). Depressed individuals can exhibit a significant lift in mood after a night of sleep deprivation. SSRIs may directly depend on the increase of central serotonergic neurotransmission for their therapeutic effect, the same system that impacts cycles of sleep and wakefulness.

Research on the effects of light therapy on seasonal affective disorder suggests that light deprivation is related to decreased activity in the serotonergic system and to abnormalities in the sleep cycle, particularly insomnia. Exposure to light also targets the serotonergic system, providing more support for the important role this system may play in depression. Sleep deprivation and light therapy both target the same brain neurotransmitter system and brain areas as antidepressant drugs, and are now used clinically to treat depression. Light therapy, sleep deprivation and sleep time displacement (sleep phase advance therapy) are being used in combination quickly to interrupt a deep depression in hospitalized patients.

Genetic factors

In 2003 *Science* published an influential study of Avshalom Caspi et al. who found that a gene-environment interaction (GxE) may explain why life stress is a predictor for depressive episodes in some individuals, but not in others, depending on an allelic variation of the serotonin-transporter-linked promoter region (5-HTTLPR). Soon after, the results were replicated by Kenneth Kendler's group, raising hopes in the psychiatric genetics community. By 2007 there were 11 replications, 3 partial replication and 3 non-replications of this proposed GxE. However, two of the largest studies were negative. Two 2009 meta-analyses were also negative; one included 14 studies, the other just five, owing to different study selection criteria. A 2010 review of studies in this area found 17 replications, 8 partial replications (interaction only in females or only with one of several types of adversity), and 9 non-replications (no interaction or an interaction in the opposite direction). It also found a systematic relationship between the method used to assess environmental adversity and the results of the studies; all studies using objective indicators or structured interviews to assess stress replicated the gene–environment interaction fully or partially, whereas all non-replications relied on brief self-report measures of adversity. This review also found that both 2009 meta-analyses were significantly biased toward negative studies.

Other hypothesized genomic influences are BDNF polymorphisms, but the replications studies have been mixed and insufficient as of 2005 for a meta-analysis. Studies also indicate an association of BDNF to suicidal behavior. However, findings from the gene-environment interactions studies suggest that the current BDNF models of depression are too simplistic. A 2008 study found interactions (biological epistasis) in the signaling pathways of the BDNF and the serotonin transporter; the BDNF Val66Met allele, which was predicted to have reduced responsitivity to serotonin, was found to exercise protective effects in individuals with the short 5-HTTLPR allele that is otherwise believed to predispose individuals to depressive episodes after stressful events. Thus, the BDNF-mediated signalling involved in neuroplastic responses to stress and antidepressants is influenced by other genetic and environmental modifiers.

Fructose malabsorbtion

A series of 50 subjects examined in an Australian study showed increased depressive scores on Beck Depression Inventory associated with reduced plasma tryptophan, due to Fructose malabsorption

Chapter 7

Evolutionary Approaches to Depression

Major depression is the leading cause of disability worldwide, and in 2000 was the fourth leading contributor to the global burden of disease (measured in DALYs); it is also an important risk factor for suicide. It is understandable, then, that clinical depression is thought to be a pathology — a major dysfunction of the brain. In most cases, rates of organ dysfunction increase with age, with low rates in adolescents and young adults, and the highest rates in the elderly. These patterns are consistent with evolutionary theories of aging which posit that selection against dysfunctional traits decreases with age (because there is a decreasing probability of surviving to later ages).

In contrast to these patterns, prevalence of clinical depression is high in all age categories, including otherwise healthy adolescents and young adults. In one study of the US population, for example, the 12 month prevalence for a major depression episode was highest in the youngest age category (15–24 year olds). The high prevalence of depression is also an outlier when compared to the prevalence of major mental retardation, autism, and schizophrenia, all with prevalence rates about one tenth that of depression, or less.

The common occurrence and persistence of a trait like clinical depression with such negative effects early in life is difficult to explain. (Rates of infectious disease are high in young people, of course, but clinical depression is not thought to be caused by an infection.) Evolutionary psychology and its application in evolutionary medicine suggest how behaviour and mental states, including seemingly harmful states such as depression, may be past adaptations to recurring reproductive problems faced by our ancestors, actually having improved however disadvantageous in the modern world, the fitness of either the individual or their relatives. It has been argued, for example, that Abraham Lincoln's life-long depression was a source of insight and strength. Some even suggest that *"we aren't designed to have happiness as our natural default"* and so a state of depression is the evolutionary norm.

The following hypotheses attempt to identify a benefit of depression that outweighs its obvious costs. All take as their starting point the fact that one of the most potent, well-established causes of major depression is a severe negative life event.

Psychic pain hypothesis

One reason depression is thought to be a pathology is that it causes so much psychic pain and distress. However, physical pain is also very distressful, yet it has an evolved function: to inform the organism that it is suffering damage, to motivate it to withdraw from the source of damage, and to learn to avoid such damage-causing circumstances in the future.

According to the psychic pain hypothesis, depression is analogous to physical pain in that it informs the sufferer that current circumstances, such as the loss of a friend, are imposing a threat to biological fitness, it motivates the sufferer to cease activities that led to the costly situation, if possible, and it causes him or her to learn to avoid similar circumstances in the future. Proponents of this view tend to focus on low mood, and regard clinical depression as a dysfunctional extreme of low mood.

Rank theory

Rank theory is the hypothesis that, if an individual is involved in a lengthy fight for dominance in a social group and is clearly losing, then depression causes the individual to back down and accept the submissive role. In doing so, the individual is protected from unnecessary harm. In this way, depression helps maintain a social hierarchy. This theory is a special case of a more general theory derived from the psychic pain hypothesis: that the cognitive response that produces modern-day depression evolved as a mechanism that allows people to assess whether they are in pursuit of an unreachable goal, and if they are, to motivate them to desist.

Honest signaling theory

Another reason depression is thought to be a pathology is that key symptoms, such as loss of interest in virtually all activities, are extremely costly to the sufferer. Biologists and economists have proposed, however, that signals with inherent costs can credibly signal information when there are conflicts of interest. In the wake of a serious negative life event, such as those that have been implicated in depression (e.g., death, divorce), "cheap" signals of need, such as crying, might not be believed when social partners have conflicts of interest. The symptoms of major depression, such as loss of interest in virtually all activities and suicidality, are inherently costly, but, as costly signaling theory requires, the costs differ for individuals in different states. For individuals who are not genuinely in need, the fitness cost of major depression is very high because it threatens the flow of fitness benefits. For individuals who are in genuine need, however, the fitness cost of major depression is low, because the individual is not generating many fitness benefits. Thus, only an individual in genuine need can afford to suffer major depression. Major depression therefore serves as an honest, or credible, signal of need.

For example, individuals suffering a severe loss such as the death of a spouse are often in need of help and assistance from others. Such individuals who have few conflicts with their social partners are predicted to experience grief—a means, in part, to signal need to

others. Such individuals who have many conflicts with their social partners, in contrast, are predicted to experience depression—a means, in part, to *credibly* signal need to others who might be skeptical that the need is genuine. *(A theologian might say that depression is like the difference between attrition and contrition. If it doesn't hurt it doesn't work).* Put in simple language, depression may function to *enforce sincerity*.

Social navigation or niche change theory

The social navigation, bargaining, or niche change hypothesis suggests that depression, operationally defined as a combination of prolonged anhedonia and psychomotor retardation or agitation, provides a focused sober perspective on socially imposed constraints hindering a person's pursuit of major fitness enhancing projects. Simultaneously, publicly displayed symptoms, which reduce the depressive's ability to conduct basic life activities, serve as a social signal of need; the signal's costliness for the depressive certifies its honesty. Finally, for social partners who find it uneconomical to respond helpfully to an honest signal of need, the same depressive symptoms also have the potential to extort relevant concessions and compromises. Depression's extortionary power comes from the fact that it retards the flow of just those goods and services such partners have come to expect from the depressive under status quo socioeconomic arrangements.

Thus depression may be a social adaptation especially useful in motivating a variety of social partners, all at once, to help the depressive initiate major fitness-enhancing changes in their socioeconomic life. There are diverse circumstances under which this may become necessary in human social life, ranging from loss of rank or a key social ally which makes the current social niche uneconomic to having a set of creative new ideas about how to make a livelihood which begs for a new niche. The social navigation hypothesis emphasizes that an individual can become tightly ensnared in an overly restrictive matrix of social exchange contracts, and that this situation sometimes necessitates a radical contractual upheaval that is beyond conventional methods of negotiation. Regarding the treatment of depression, this hypothesis calls into question any assumptions by the clinician that the typical cause of depression is related to maladaptive perverted thinking processes or other purely endogenous sources. The social navigation hypothesis calls instead for analysis of the depressive's talents and dreams, identification of relevant social constraints (especially those with a relatively diffuse non-point source within the social network of the depressive), and practical social problem-solving therapy designed to relax those constraints enough to allow the depressive to move forward with their life under an improved set of social contracts. This theory has been the subject of criticism.

Bargaining theory

Depression is not only costly to the sufferer, it also imposes a significant burden on family, friends, and society at large—yet another reason it is thought to be pathological. Yet if sufferers of depression have real but unmet needs, they might have to provide an incentive to others to address those needs.

The bargaining theory of depression is similar to the honest signaling, niche change, and social navigation theories of depression described above. It draws on theories of labor strikes developed by economists to basically add one additional element to honest signaling theory: The fitness of social partners is generally correlated. When a wife suffers depression and reduces her investment in offspring, for example, the husband's fitness is also put at risk. Thus, not only do the symptoms of major depression serve as costly and therefore honest signals of need, they also compel reluctant social partners to respond to that need in order to prevent their own fitness from being reduced.

Prevention of infection

It has been hypothesized that depression is an evolutionary adaptation because it helps prevent infection in both the affected individual and his/her kin.

First, the associated symptoms of depression, such as inactivity and lethargy, encourage the affected individual to rest. Energy conserved through such methods is highly crucial, as immune activation against infections is relatively costly; there must be, for instance, a 10% increase in metabolic activity for even a 1℃ change in body temperature. Therefore, depression allows one to conserve and allocate energy to the immune system more efficiently.

Depression further prevents infection by discouraging social interactions and activities that may result in exchange of infections. For example, the loss of interest discourages one from engaging in sexual activity, which, in turn, prevents the exchange of sexually transmitted diseases. Similarly, depressed mothers may interact less with their children, reducing the probability of the mother infecting her kin. Lastly, the lack of appetite associated with depression may also reduce exposure to food-borne parasites.

Analytical rumination hypothesis

This hypothesis suggests that depression is an adaptation that causes the affected individual to concentrate his or her attention and focus on a complex problem in order to analyze and solve it.

One way depression increases the individual’s focus on a problem is by inducing rumination. Depression activates the left ventrolateral prefrontal cortex, which increases attention control and maintains problem-related information in an “active, accessible state” referred to as “working memory,” or WM. As a result, depressed individuals have been shown to ruminate, reflecting on the reasons for their current problems. Feelings of regret associated with depression also cause individuals to reflect and analyze past events in order to determine why they happened and how they could have been prevented.

Another way depression increases an individual’s ability to concentrate on a problem is by reducing distraction from the problem. For example, anhedonia, which is often associated with depression, decreases an individual’s desire to participate in activities that provide short-term rewards, and instead, allows the individual to concentrate on long-

term goals. In addition, “psychomotory changes,” such as solitariness, decreased appetite, and insomnia also reduce distractions. For instance, insomnia enables conscious analysis of the problem to be maintained by preventing sleep from disrupting such processes. Likewise, solitariness, lack of physical activity, and lack of appetite all eliminate sources of distraction, such as social interactions, navigation through the environment, and “oral activity,” which disrupt stimuli from being processed.

Social risk hypothesis

This hypothesis explains the evolutionary origin of depression in the ancestral context in which depression was an adaptation that enabled an individual to maintain social ties critical for survival and reproduction. During the Pleistocene period, for instance, such social ties were vital in food foraging and protection from predators.

Depression, resulting from one’s loss of “Social Attention Holding Power,” or SAHP, may have signalled the individual's submissiveness to the more dominant males of the social group through associated symptoms, such as low confidence and anxiety. This, in turn, reduced tension among group members, and enabled bonds to be maintained. Secondly, depression may also have served to signal other members of an individual’s need for aid and desire to reform lost bonds.

Behavioral shutdown model

If an organism faces more risk or expenditure than reward from activities, the best evolutionary strategy may be to withdraw from them. The behavioral shutdown model proposes that emotional pain, like physical pain, serves a useful adaptive purpose. Negative emotions like disappointment, sadness, grief, fear, anxiety, anger, and guilt are described as "evolved strategies that allow for the identification and avoidance of specific problems, especially in the social domain." Depression is characteristically associated with anhedonia and lack of energy, and those experiencing it are risk-aversive and perceive more negative and pessimistic outcomes because they are focused on preventing further loss. Although the model views depression as an adaptive response, it does not suggest that it is beneficial by the standards of current society; but it does suggest that many approaches to depression treat symptoms rather than causes, and underlying social problems need to be addressed.

Possibilities of depression as a dysregulated adaptation

Depression, especially in the modern context, may not necessarily be adaptive. The ability to feel pain, have diarrhea, and experience depression, are adaptive defense mechanisms, but when they are “too easily triggered, too intense, or long lasting,” they can become “dysregulated.” In such a case, defense mechanisms, too, can become diseases, such as “chronic pain or dehydration from diarrhea.” Depression, which may be a similar kind of defense mechanism, may have become dysregulated as well.

Chapter 8

Mood Disorder

Mood disorder	
ICD-10	F30.-F39.
ICD-9	296
MeSH	D019964

Mood disorder is the term designating a group of diagnoses in the Diagnostic and Statistical Manual of Mental Disorders (DSM IV TR) classification system where a disturbance in the person's mood is hypothesized to be the main underlying feature. The classification is known as *mood (affective) disorders* in ICD 10.

English psychiatrist Henry Maudsley proposed an overarching category of *affective disorder*. The term was then replaced by *mood disorder*, as the latter term refers to the underlying or longitudinal emotional state, whereas the former refers to the external expression observed by others.

Two groups of mood disorders are broadly recognized; the division is based on whether the person has ever had a manic or hypomanic episode. Thus, there are depressive disorders, of which the best known and most researched is **major depressive disorder (MDD)** commonly called *clinical depression* or *major depression*, and **bipolar disorder (BD)**, formerly known as *manic depression* and characterized by intermittent episodes of mania or hypomania, usually interlaced with depressive episodes.

Classification

Depressive disorders

- **Major depressive disorder** (**MDD**), commonly called major depression, unipolar depression, or clinical depression, where a person has one or more major depressive episodes. After a single episode, Major Depressive Disorder (single episode) would be diagnosed. After more than one episode, the diagnosis becomes Major Depressive Disorder (Recurrent). Depression without periods of

mania is sometimes referred to as *unipolar depression* because the mood remains at one emotional state or "pole".

Individuals with a major depressive episode or major depressive disorder are at increased risk for suicide. Seeking help and treatment from a health professional dramatically reduces the individual's risk for suicide. Studies have demonstrated that asking if a depressed friend or family member has thought of committing suicide is an effective way of identifying those at risk, and it does not "plant" the idea or increase an individual's risk for suicide in any way. Epidemiological studies carried out in Europe suggest that at this moment, roughly 8.5 percent of the worlds population are suffering from a depressive disorder. No age group seems to be exempt from depression and studies have found that depression appears in infants as young as 6 months old who have been separated from their mothers.
Diagnosticians recognize several subtypes or course specifiers:

- *Atypical depression* (*AD*) is characterized by mood reactivity (paradoxical anhedonia) and positivity, significant weight gain or increased appetite ("comfort eating"), excessive sleep or somnolence (hypersomnia), a sensation of heaviness in limbs known as leaden paralysis, and significant social impairment as a consequence of hypersensitivity to perceived interpersonal rejection. Difficulties in measuring this subtype have led to questions of its validity and prevalence.

- *Melancholic depression* is characterized by a loss of pleasure (anhedonia) in most or all activities, a failure of reactivity to pleasurable stimuli, a quality of depressed mood more pronounced than that of grief or loss, a worsening of symptoms in the morning hours, early morning waking, psychomotor retardation, excessive weight loss (not to be confused with anorexia nervosa), or excessive guilt.

- *Psychotic major depression* (*PMD*), or simply psychotic depression, is the term for a major depressive episode, particularly of melancholic nature, where the patient experiences psychotic symptoms such as delusions or, less commonly, hallucinations. These are most commonly mood-congruent (content coincident with depressive themes).

- *Catatonic depression* is a rare and severe form of major depression involving disturbances of motor behavior and other symptoms. Here the person is mute and almost stuporose, and either immobile or exhibits purposeless or even bizarre movements. Catatonic symptoms can also occur in schizophrenia, a manic episode, or be due to neuroleptic malignant syndrome.

- *Postpartum depression* (*PPD*) is listed as a course specifier in DSM-IV-TR; it refers to the intense, sustained and sometimes disabling depression

experienced by women after giving birth. Postpartum depression, which has incidence rate of 10–15%, typically sets in within three months of labor, and lasts as long as three months. It is quite common for women to experience a short term feeling of tiredness and sadness in the first few weeks after giving birth; however, postpartum depression is different because it can cause significant hardship and impaired functioning at home, work, or school as well as possibly difficulty in relationships with family members, spouses, friends, or even problems bonding with the newborn. In the treatment of postpartum major depressive disorders and other unipolar depressions in women who are breastfeeding, nortriptyline, paroxetine (Paxil), and sertraline (Zoloft) are generally considered to be the preferred medications.

- *Seasonal affective disorder* (*SAD*), also known as "winter depression" or "winter blues", is a specifier. Some people have a seasonal pattern, with depressive episodes coming on in the autumn or winter, and resolving in spring. The diagnosis is made if at least two episodes have occurred in colder months with none at other times over a two-year period or longer. It is commonly hypothesised that people who live at higher latitudes tend to have less sunlight exposure in the winter and therefore experience higher rates of SAD, but the epidemiological support for this proposition is not strong (and latitude is not the only determinant of the amount of sunlight reaching the eyes in winter). SAD is also more prevalent in people who are younger and typically affects more females than males.

- **Dysthymia**, which is a chronic, different mood disturbance where a person reports a low mood almost daily over a span of at least two years. The symptoms are not as severe as those for major depression, although people with dysthymia are vulnerable to secondary episodes of major depression (sometimes referred to as *double depression*). The treatment of dysthymia is largely the same as for major depression, including antidepressant medications and psychotherapy.

- **Depressive Disorder Not Otherwise Specified** (**DD-NOS**) is designated by the code *311* for depressive disorders that are impairing but do not fit any of the officially specified diagnoses. According to the DSM-IV, DD-NOS encompasses *"any depressive disorder that does not meet the criteria for a specific disorder."* It includes the research diagnoses of *recurrent brief depression*, and *minor depressive disorder* listed below.

    - *Recurrent brief depression* (*RBD*), distinguished from major depressive disorder primarily by differences in duration. People with RBD have depressive episodes about once per month, with individual episodes lasting less than two weeks and typically less than 2–3 days. Diagnosis of RBD requires that the episodes occur over the span of at least one year and, in female patients, independently of the menstrual cycle. People with

clinical depression can develop RBD, and vice versa, and both illnesses have similar risks.

- *Minor depressive disorder*, or simply minor depression, which refers to a depression that does not meet full criteria for major depression but in which at least two symptoms are present for two weeks.

Bipolar disorders

- **Bipolar disorder** (**BD**), a mood disorder formerly known as "manic depression" and described by alternating periods of mania and depression (and in some cases rapid cycling, mixed states, and psychotic symptoms). Subtypes include:

  - *Bipolar I* is distinguished by the presence or history of one or more manic episodes or mixed episodes with or without major depressive episodes. A depressive episode is not required for the diagnosis of Bipolar I disorder, but depressive episodes are often part of the course of the illness.
  - *Bipolar II* consisting of recurrent intermittent hypomanic and depressive episodes.
  - *Cyclothymia* is a form of bipolar disorder, consisting of recurrent hypomanic and dysthymic episodes, but no full manic episodes or full major depressive episodes.
  - *Bipolar Disorder Not Otherwise Specified* (*BD-NOS*), sometimes called "sub-threshold" bipolar, indicates that the patient suffers from some symptoms in the bipolar spectrum (e.g. manic and depressive symptoms) but does not fully qualify for any of the three formal bipolar DSM-IV diagnoses mentioned above.

  It is estimated that roughly one percent of the adult population suffers from bipolar I, roughly one percent of the adult population suffers from bipolar II or cyclothymia, and somewhere between two and five percent suffer from "sub-threshold" forms of bipolar disorder.

Substance induced mood disorders

A mood disorder can be classified as substance-induced if its etiology can be traced to the direct physiologic effects of a psychoactive drug or other chemical substance, or if the development of the mood disorder occurred contemporaneously with substance intoxication or withdrawal. Alternately, an individual may have a mood disorder coexisting with a substance abuse disorder. Substance-induced mood disorders can have features of a manic, hypomanic, mixed, or depressive episode. Most substances can induce a variety of mood disorders. For example, stimulants such as amphetamine, methamphetamine, and cocaine can cause manic, hypomanic, mixed, and depressive episodes.

Alcohol induced mood disorders

High rates of major depressive disorder occur in heavy drinkers and those with alcoholism. Controversy has previously surrounded whether those who abused alcohol and developed depression were self-medicating their pre-existing depression, but recent research has concluded that, while this may be true in some cases, alcohol misuse directly causes the development of depression in a significant number of heavy drinkers. High rates of suicide also occur in those who have alcohol-related problems. It is usually possible to differentiate between alcohol-related depression and depression which is not related to alcohol intake by taking a careful history of the patient. Depression and other mental health problems associated with alcohol misuse may be due to distortion of brain chemistry, as they tend to improve on their own after a period of abstinence.

Benzodiazepine induced mood disorders

The long-term use of benzodiazepines, such as Valium and Librium, may have a similar effect on the brain as alcohol, and are also implicated in depression. Major depressive disorder can also develop as a result of chronic use of benzodiazepines or as part of a protracted withdrawal syndrome. Benzodiazepines are a class of medication which are commonly used to treat insomnia, anxiety and muscular spasms. As with alcohol, the effects of benzodiazepine on neurochemistry, such as decreased levels of serotonin and norepinephrine, are believed to be responsible for the increased depression. Major depressive disorder may also occur as part of the benzodiazepine withdrawal syndrome. In a long-term follow-up study of patients dependent on benzodiazepines, it was found that 10 people (20%) had taken drug overdoses while on chronic benzodiazepine medication despite only two people ever having had any pre-existing depressive disorder. A year after a gradual withdrawal program, no patients had taken any further overdoses. Depression resulting from withdrawal from benzodiazepines usually subsides after a few months but in some cases may persist for 6–12 months.

Interferon-alpha induced mood disorders

Combination therapy with interferon-α and ribavirin for chronic hepatitis C virus (HCV) infection may induce major depression. In the study by Leutscher et al, evaluating 325 chronically HCV infected patients undergoing antiviral therapy, it was observed that (1) depressive symptoms among patients undergoing HCV therapy are commonly overlooked by routine clinical interviews, (2) the emergence of depression compromises the outcome of HCV therapy, and (3) the Major Depression Inventory (MDI) scale may be useful in identifying patients at risk for treatment-induced depression.

Origin

A number of authors have suggested that mood disorders are an evolutionary adaptation. A low or depressed mood can increase an individual's ability to cope with situations in which the effort to pursue a major goal could result in danger, loss, or wasted effort. In such situations, low motivation may give an advantage by inhibiting certain actions. This

theory helps to explain why mood disorders are so prevalent, and why they so often strike people during their peak reproductive years. These characteristics would be difficult to understand if depression were a dysfunction.

A depressed mood is a predictable response to certain types of life occurrences, such as loss of status, divorce, or death of a child or spouse. These are events that signal a loss of reproductive ability or potential, or that did so in humans' ancestral environment. A depressed mood can be seen as an adaptive response, in the sense that it causes an individual to turn away from the earlier (and reproductively unsuccessful) modes of behavior.

A depressed mood is common during illnesses, such as influenza. It has been argued that this is an evolved mechanism that assists the individual in recovering by limiting his/her physical activity. The occurrence of low-level depression during the winter months, or seasonal affective disorder, may have been adaptive in the past, by limiting physical activity at times when food was scarce. It is argued that humans have retained the instinct to experience low mood during the winter months, even if the availability of food is no longer determined by the weather.

Sociocultural aspects

Kay Redfield Jamison and others have explored the possible links between mood disorders—especially bipolar disorder—and creativity. It has been proposed that a "ruminating personality type may contribute to both [mood disorders] and art." The relationship between depression and creativity appears to be especially strong among poets.

Epidemiology

According to a substantial amount of epidemiology studies conducted, women are twice as likely to develop mood disorders as men.

Chapter 9

Sleep Medicine

An example of a sleep diary layout

Sleep medicine is a medical specialty or subspecialty devoted to the diagnosis and therapy of sleep disturbances and disorders. From the middle of the 20th century, research has provided increasing knowledge and answered many questions about sleep-wake functioning. The rapidly evolving field has become a recognized medical subspecialty in some countries. Dental sleep medicine also qualifies for board certification in some countries. Properly organized, minimum 12-month, postgraduate training programs are still being defined in the United States. In some countries, the sleep researchers and the doctors who treat patients may be the same people.

The first sleep clinics in the United States were established in the 1970s by interested doctors and technicians; the study, diagnosis and treatment of obstructive sleep apnea were their first tasks. As late as 1999, virtually any American doctor, with no specific training in sleep medicine, could open a sleep laboratory.

Disorders and disturbances of sleep are widespread and can have significant consequences for affected individuals as well as economic and other consequences for society. The US National Transportation Safety Board has, according to Dr. Charles Czeisler, member of the Institute of Medicine and Director of the Harvard University Medical School Division of Sleep Medicine at Brigham and Women's Hospital, discovered that the leading cause of fatal-to-the-driver heavy truck crashes is fatigue-

related (fatigue – 31%, alcohol and other drug use – 29%), and sleep deprivation has been a significant factor in dramatic accidents, such as the Exxon Valdez oil spill, the nuclear incidents at Chernobyl and Three Mile Island and the explosion of the space shuttle *Challenger*.

Scope and classification

Competence in sleep medicine requires an understanding of a plethora of very diverse disorders, many of which present with similar symptoms such as excessive daytime sleepiness, which, in the absence of volitional sleep deprivation, "is almost inevitably caused by an identifiable and treatable sleep disorder," such as sleep apnea, narcolepsy, idiopathic central nervous system (CNS) hypersomnia, Kleine-Levin syndrome, menstrual-related hypersomnia, idiopathic recurrent stupor, or circadian rhythm disturbances. Another common complaint is insomnia, a set of symptoms that can have many causes, physical and mental. Management in the varying situations differs greatly and cannot be undertaken without a correct diagnosis.

ICSD, *The International Classification of Sleep Disorders*, was restructured in 1990, in relation to its predecessor, to include only one code for each diagnostic entry and to classify disorders by pathophysiologic mechanism, as far as possible, rather than by primary complaint. Training in sleep medicine is multidisciplinary, and the present structure was chosen to encourage a multidisciplinary approach to diagnosis. Sleep disorders often do not fit neatly into traditional classification; differential diagnoses cross medical systems. Minor revisions and updates to the ICSD were made in 1997 and in following years. The present classification system in fact follows the groupings suggested by Nathaniel Kleitman, the "father of sleep research," in his seminal 1939 book *Sleep and Wakefulness*.

The revised ICSD, ICSD-R, placed the primary sleep disorders in the subgroups (1) dyssomnias, which include those that produce complaints of insomnia or excessive sleepiness, and (2) the parasomnias, which do not produce those primary complaints but intrude into or occur during sleep. A further subdivision of the dyssomnias preserves the integrity of circadian rhythm sleep disorders, as was mandated by about 200 doctors and researchers from all over the world who participated in the process between 1985–1990. The last two subgroups were (3) the medical or psychiatric sleep disorder section and (4) the proposed new disorders section. The authors found the heading "medical or psychiatric" less than ideal but better than the alternative "organic or non-organic," which seemed more likely to change in the future. Detailed reporting schemes aimed to provide data for further research. A second edition, called ICSD-2, was published in 2005.

MeSH, *Medical Subject Headings*, a service of the US National Library of Medicine and the National Institutes of Health, uses similar broad categories: (1) dyssomnias, including narcolepsy, apnea, and the circadian rhythm sleep disorders, (2) parasomnias, which include, among others, bruxism (tooth-grinding), sleepwalking and bedwetting, and (3) sleep disorders caused by medical or psychiatric conditions. The system used produces

"trees," approaching each diagnosis from up to several angles such that each disorder may be known by several codes.

DSM-IV-TR, the *Diagnostic and Statistical Manual of Mental Disorders, Fourth Edition, Text Revision*, using the same diagnostic codes as the *International Statistical Classification of Diseases and Related Health Problems* (ICD), divides sleep disorders into three groups: (1) primary sleep disorders, both the dyssomnias and the parasomnias, presumed to result from an endogenous disturbance in sleep-wake generating or timing mechanisms, (2) those secondary to mental disorders and (3) those related to a general medical condition or substance abuse.

Recent thinking opens for a common cause for mood and sleep disorders occurring in the same patient; a 2010 review states that, in humans, "single nucleotide polymorphisms in *Clock* and other clock genes have been associated with depression" and that the "evidence that mood disorders are associated with disrupted or at least inappropriately timed circadian rhythms suggests that treatment strategies or drugs aimed at restoring 'normal' circadian rhythmicity may be clinically useful."

History

A 16th-century physician wrote that many laborers dozed off exhausted at the start of each night; sexual intercourse with their wives typically occurring in the *watching period*, after a recuperative first sleep. Anthropologists find that isolated societies without electric light sleep in a variety of patterns; seldom do they resemble our modern habit of sleeping in one single eight-hour bout. Much has been written about dream interpretation, from biblical times to Freud, but sleep itself was historically seen as a passive state of not-awake.

The concept of sleep medicine belongs to the second half of the 20th century. Due to the rapidly increasing knowledge about sleep, including the growth of the research field chronobiology from about 1960 and the discoveries of REM sleep (1952–53) and sleep apnea (first described in the medical literature in 1965), the medical importance of sleep was recognized. The medical community began paying more attention than previously to primary sleep disorders, such as sleep apnea, as well as the role and quality of sleep in other conditions. By the 1970s in the US, and in many western nations within the two following decades, clinics and laboratories devoted to the study of sleep and the treatment of its disorders had been founded. Most sleep doctors were primarily concerned with apnea; some were experts in narcolepsy. There was as yet nothing to restrict the use of the title "sleep doctor," and a need for standards arose.

Basic medical training has paid little attention to sleep problems; according to Benca in her review *Diagnosis and Treatment of Chronic Insomnia* (2005), most doctors are "not well trained with respect to sleep and sleep disorders," and a survey in 1990–91 of 37 American medical schools showed that sleep and sleep disorders were "covered" in less than two (2) hours of total teaching time, on average. Benca's review cites a 2002 survey by Papp et al. of more than 500 primary care physicians who self-reported their

knowledge of sleep disorders as follows: Excellent – 0%; Good – 10%, Fair – 60%; and Poor – 30%. The review of more than 50 studies indicates that both doctors and patients appear reluctant to discuss sleep complaints, in part because of perceptions that treatments for insomnia are ineffective or associated with risks, and:

> “ Physicians may avoid exploring problems such as sleep difficulties in order to avoid having to deal with issues that could take up more than the normal allotted time for a patient. ”

Also, an editorial in the American College of Chest Physicians' (pulmonologists') journal *CHEST* in 1999 was quite concerned about the *Conundrums in Sleep Medicine*. The author, then chair of her organization's Sleep Section, asked "What is required to set up a sleep laboratory? Money and a building! Anyone can open a sleep laboratory, and it seems that just about everyone is." On the accreditation process for sleep laboratories, she continues: "This accreditation, however, is currently not required by most states, or more importantly, by most insurance carriers for reimbursements... There is also an American Board of Sleep Medicine (ABSM) that certifies individuals as sleep specialists. This certification presumably makes those individuals more qualified to run a sleep laboratory; however, the certification is not required to run a laboratory or to read sleep studies." Her concern at the turn of the century was:

> “ Not all patients with hypersomnia have sleep apnea, and other diagnoses may be missed if the physician is only trained to diagnose and treat sleep apnea. Also, when a physician runs a sleep laboratory, they are "assumed" to be a sleep expert and are asked to evaluate and treat all types of sleep disorders when they are not adequately trained to do so. ”

In the UK, knowledge of sleep medicine and possibilities for diagnosis and treatment seem to lag. Guardian.co.uk quotes the director of the Imperial College Healthcare Sleep Centre: "One problem is that there has been relatively little training in sleep medicine in this country – certainly there is no structured training for sleep physicians." The Imperial College Healthcare site shows attention to obstructive sleep apnea syndrome (OSA) and very few other disorders, specifically not including insomnia.

Training and certification

Worldwide

The World Federation of Sleep Research & Sleep Medicine Societies (WFSRSMS) was founded in 1987. As its name implies, members are concerned with basic and clinical research as well as medicine. Member societies in the Americas are the American Academy of Sleep Medicine (AASM), the Sleep Research Society of the United States (SRS), the Canadian Sleep Society (CSS) and the Federation of Latin American Sleep

Societies (FLASS). WFSRSMS publishes the *Journal of Sleep Research*, the *Journal of Clinical Sleep Medicine*, *SLEEP* and *Sleep and Biological Rhythms* and promotes both sleep research and physician training and education.

Africa

The Colleges of Medicine of South Africa (CMSA) provide the well-defined specialty Diploma in Sleep Medicine of the College of Neurologists of South Africa: DSM(SA), which was first promulgated by the Health Professions Council in 2007. The newly formed South African Society of Sleep Medicine (SASSM) was launched at its inaugural congress in February 2010. The society's membership is diverse; it includes general practitioners, ENT surgeons, pulmonologists, cardiologists, endocrinologists and psychiatrists.

Asia

WFSRSMS members in Asia include the Australasian Sleep Association (ASA) of New Zealand and Australia and the Asian Sleep Research Society (ASRS), an umbrella organization for the societies of several Asian nations.

Europe

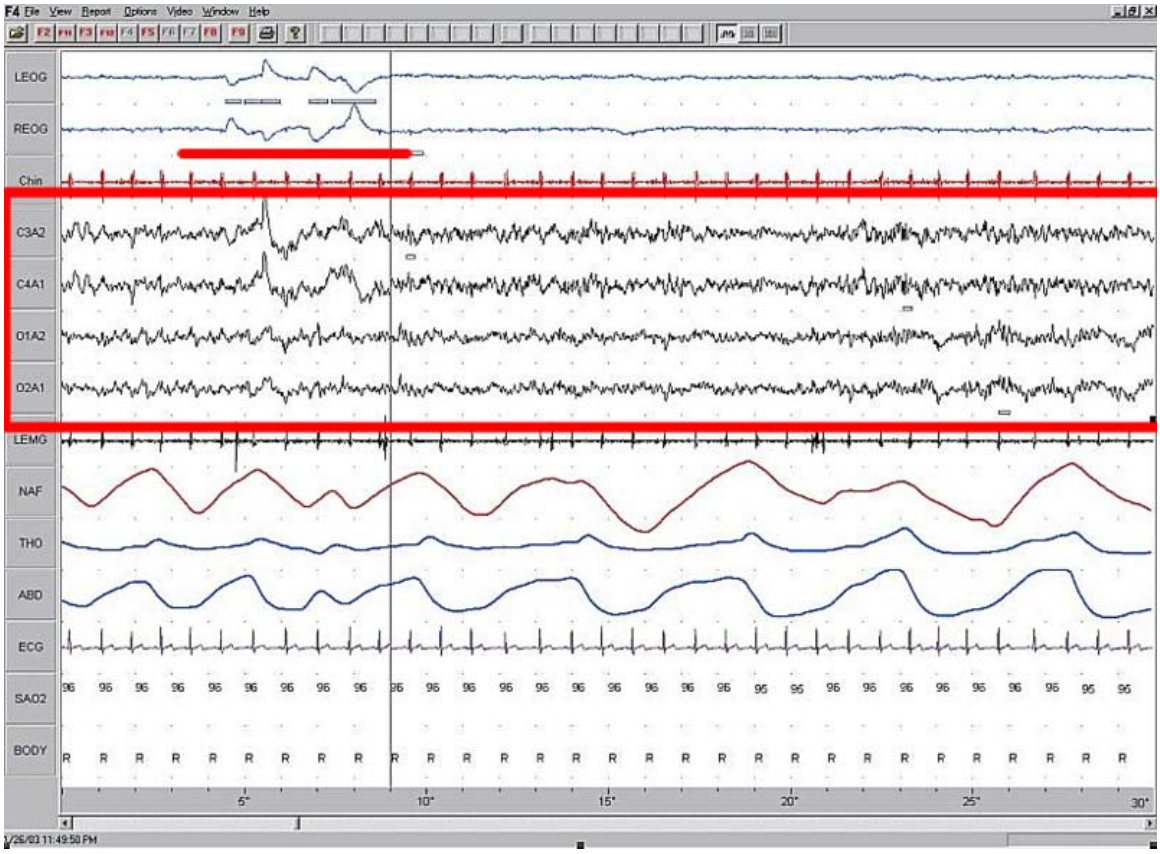
The European Sleep Research Society (ESRS) is a member of the WFSRSMS. The Assembly of National Sleep Societies (ANSS), which includes both medical and scientific organizations from 26 countries as of 2007, is a formal body of the ESRS. The ESRS has published *European Accreditation Guidelines for SMCs* (Sleep Medicine Centres), the first of several proposed guidelines to coordinate and promote sleep science and medicine in Europe.

United States

The American Academy of Sleep Medicine (AASM), founded in 1978, administered the certification process and sleep medicine examination for doctors until 1990. Its independent daughter entity the American Board of Sleep Medicine (ABSM) was incorporated in 1991 and took over the aforementioned responsibilities. As of 2007, the ABSM ceased administering its examination, as it conceded that an examination process recognized by the American Board of Medical Specialties (ABMS) was advantageous to the field. Candidates who passed the ABSM exam in 1978–2006 retain lifetime certification as Diplomates of that organization.

The American Board of Psychiatry and Neurology (ABPN), and the corresponding boards of Internal Medicine, of Pediatrics, and of Otolaryngology (ear, nose and throat, ENT) now administer collectively the Sleep Medicine Certification exam for their members. Each board supervises the required 12 months of formal training for its candidates, while the exam is administered to all of them at the same time in the same place. For the first five years, 2007–2011, during "grandfathering," there is a "practice

pathway" for ABSM certified specialists. Additional, coordinated requirements are to be added after 2011. The ABPN provides information about the pathways, requirements and the exam on its website.



Detail from a polysomnogram, one of the tools used by specialists in sleep medicine

Sleep medicine is now a recognized subspecialty within internal medicine, family medicine, pediatrics, otolaryngology, psychiatry and neurology in the US. Certification in Sleep Medicine by the several "Member Boards" of the ABMS shows that the specialist:

> “ has demonstrated expertise in the diagnosis and management of clinical conditions that occur during sleep, that disturb sleep, or that are affected by disturbances in the wake–sleep cycle. This specialist is skilled in the analysis and interpretation of comprehensive polysomnography, and well-versed in emerging research and management of a sleep laboratory. ”

Pulmonologists, already subspecialists within internal medicine, may be accepted to sit for the board and be certified in Sleep Medicine after just a six-month fellowship, building on their knowledge of sleep-related breathing problems, rather than the usual twelve-month fellowship required of other specialists.

Sleep dentistry (bruxism, snoring and sleep apnea), while not recognized as one of the nine dental specialties, qualifies for board-certification by the American Board of Dental Sleep Medicine (ABDSM). The resulting Diplomate status is recognized by the AASM, and these dentists are organized in the Academy of Dental Sleep Medicine (USA). The qualified dentists collaborate with sleep doctors at accredited sleep centers and can provide several types of oral appliances or upper airway surgery to treat or manage sleep-related breathing disorders as well as tooth-grinding and clenching.

Laboratories for sleep-related breathing disorders are accredited by the AASM, and are required to follow the *Code of Medical Ethics* of the American Medical Association. The new and very detailed *Standards for Accreditation* are available online. Sleep disorder centers, or clinics, are accredited by the same body, whether hospital-based, university-based or "freestanding"; they are required to provide testing and treatment for *all* sleep disorders and to have on staff a sleep specialist who has been certified by the American Board of Sleep Medicine and otherwise meet similar standards.

Diagnostic methods

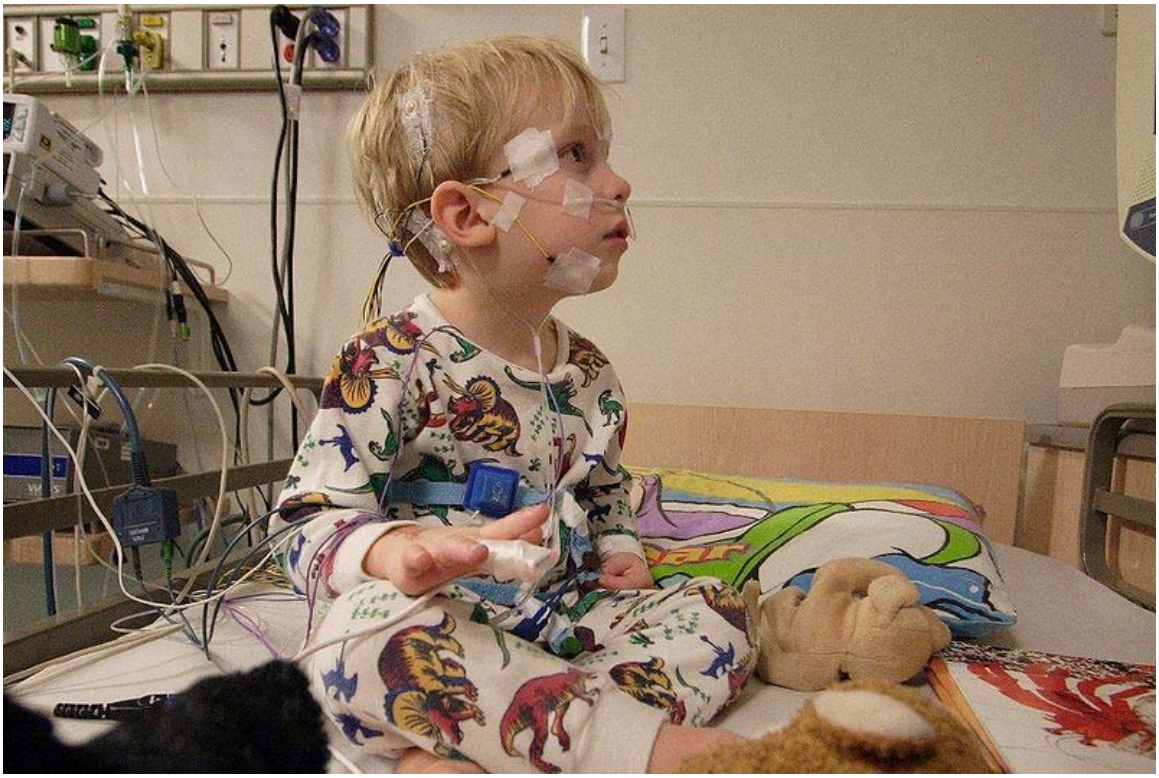
The taking of a thorough medical history while keeping in mind alternative diagnoses and the possibility of more than one ailment in the same patient is the first step. Symptoms for very different sleep disorders may be similar and it must be determined whether any psychiatric problems are primary or secondary.

The patient history includes previous attempts at treatment and coping and a careful medication review. Differentiation of transient from chronic disorders and primary from secondary ones influences the direction of evaluation and treatment plans.

The Epworth Sleepiness Scale (ESS), designed to give an indication of sleepiness and correlated with sleep apnea, or other questionnaires designed to measure excessive daytime sleepiness, are diagnostic tools that can be used repeatedly to measure results of treatment.

A sleep diary, also called sleep log or sleep journal, kept by a patient at home for at least two weeks, while subjective, may help determine the extent and nature of sleep disturbance and the level of alertness in the normal environment. A parallel journal kept by a parent or bed partner, if any, can also be helpful. Sleep logs also can be used for self-monitoring and in connection with behavioral and other treatment. The image at the top of this page, with nighttime in the middle and the weekend in the middle, shows a layout that can aid in noticing trends

An actigraph unit is a motion-sensing device worn on the wrist, generally for one week. It gives a gross picture of sleep-wake cycles and is often used to verify the sleep diary. It is cost-efficient when full polysomnography is not required.



Pediatric polysomnography

Polysomnography is performed in a sleep laboratory while the patient sleeps, preferably at his or her usual sleeping time. The polysomnogram (PSG) objectively records sleep stages and respiratory events. It shows multiple channels of electroencephalogram (EEG), electrooculogram (EOG), electrocardiogram (ECG), nasal and oral airflow, abdominal, chest and leg movements and blood oxygen levels. A single part of a polysomnogram is sometimes measured at home with portable equipment, for example oximetry, which records blood oxygen levels throughout the night. Polysomnography is not routinely used in the evaluation of patients with insomnia or circadian rhythm disorders, except as needed to rule out other disorders. It will usually be a definitive test for sleep apnea.

A Multiple Sleep Latency Test (MSLT) is often performed during the entire day after polysomnography while the electrodes and other equipment are still in place. The patient is given nap opportunities every second hour; the test measures the number of minutes it takes from the start of a daytime nap period to the first signs of sleep. It is a measure of daytime sleepiness; it also shows whether REM sleep is achieved in a short nap, a typical indication of narcolepsy.

Imaging studies may be performed if a patient is to be evaluated for neurodegenerative disease or to determine the obstruction in obstructive sleep apnea.

Treatments

When sleep complaints are secondary to pain, other medical or psychiatric diagnoses, or substance abuse, it may be necessary to treat both the underlying cause and the sleep problems.

When the underlying cause of sleep problems is not immediately obvious, behavioral treatments are usually the first suggested. These range from patient education about sleep hygiene to cognitive behavioral therapy (CBT). Studies of both younger and older adults have compared CBT to medication and found that CBT should be considered a first-line and cost-effective intervention for chronic insomnia, not least because gains may be maintained at long-term follow-up. Sleep physicians and psychologists, at least in the US, are not in agreement about who should perform CBT nor whether sleep centers should be required to have psychologists on staff. Behavioral therapies include progressive relaxation, stimulus control (to reassociate the bed with sleepiness), limiting time-in-bed to increase sleep efficiency and debunking misconceptions about sleep.

Walgreens brand melatonin

Pharmacology is necessary for some conditions. Medication may be useful for acute insomnia and for some of the parasomnias. It is almost always needed, along with scheduled short naps and close follow-up, in the treatment of narcolepsy and idiopathic hypersomnia.

Chronic circadian rhythm disorders, the most common of which is delayed sleep phase disorder, may be managed by specifically timed bright light therapy, timed oral administration of the hormone melatonin, and/or chronotherapy. Stimulants may also be prescribed. When these therapies are unsuccessful, counseling may be indicated to help a person adapt to and live with the condition. People with these disorders who have chosen a lifestyle in conformity with their sleeping schedules have no need of treatment, though they may need the diagnosis in order to avoid having to meet for appointments or meetings during their sleep time.

A CPAP machine

Continuous positive airway pressure (CPAP) machines and oral appliances are used nightly at home to manage sleep-related breathing disorders such as apnea. Occasionally, upper airway surgery is indicated. In mild cases in obese people, weight reduction may be sufficient. The treatments prevent airway collapse, which interrupts breathing during sleep.

Chapter 10

Sleep Disorder

Sleep disorder	
ICD-10	F51., G47.
ICD-9	307.4, 327, 780.5
DiseasesDB	26877
eMedicine	med/609
MeSH	D012893

A **sleep disorder** (somnipathy) is a medical disorder of the sleep patterns of a person or animal. Some sleep disorders are serious enough to interfere with normal physical, mental and emotional functioning. A test commonly ordered for some sleep disorders is the polysomnography.

Disruptions in sleep can be caused by a variety of issues, from teeth grinding (bruxism) to night terrors. When a person suffers from difficulty in sleeping with no obvious cause, it is referred to as insomnia. In addition, sleep disorders may also cause sufferers to sleep excessively, a condition known as hypersomnia. Management of sleep disturbances that are secondary to mental, medical, or substance abuse disorders should focus on the underlying conditions.

Common disorders

The most common sleep disorders include:

- Primary insomnia: Chronic difficulty in falling asleep and/or maintaining sleep when no other cause is found for these symptoms.
- Bruxism: Involuntarily grinding or clenching of the teeth while sleeping.
- Delayed sleep phase syndrome (DSPS): inability to awaken and fall asleep at socially acceptable times but no problem with sleep maintenance, a disorder of circadian rhythms. (Other such disorders are advanced sleep phase syndrome (ASPS), non-24-hour sleep-wake syndrome (Non-24), and irregular sleep wake

rhythm, all much less common than DSPS, as well as the transient jet lag and shift work sleep disorder.)

- Hypopnea syndrome: Abnormally shallow breathing or slow respiratory rate while sleeping.
- Narcolepsy: Excessive daytime sleepiness (EDS) often culminating in falling asleep spontaneously but unwillingly at inappropriate times.
- Cataplexy: a sudden weakness in the motor muscles that can result in collapse to the floor.
- Night terror: *Pavor nocturnus*, sleep terror disorder: abrupt awakening from sleep with behavior consistent with terror.
- Parasomnias: Disruptive sleep-related events involving inappropriate actions during sleep; sleep walking and night-terrors are examples.
- Periodic limb movement disorder (PLMD): Sudden involuntary movement of arms and/or legs during sleep, for example kicking the legs. Also known as nocturnal myoclonus..
- Rapid eye movement behavior disorder (RBD): Acting out violent or dramatic dreams while in REM sleep.
- Restless legs syndrome (RLS): An irresistible urge to move legs. RLS sufferers often also have PLMD.
- Situational circadian rhythm sleep disorders: shift work sleep disorder (SWSD) and jet lag.
- Sleep Apnea, and mostly Obstructive sleep apnea: Obstruction of the airway during sleep, causing lack of sufficient deep sleep; often accompanied by snoring. Other forms of sleep apnea are less common.
- Sleep paralysis: is characterized by temporary paralysis of the body shortly before or after sleep. Sleep paralysis may be accompanied by visual, auditory or tactile hallucinations. Not a disorder unless severe. Often seen as part of Narcolepsy.
- Sleepwalking or *somnambulism*: Engaging in activities that are normally associated with wakefulness (such as eating or dressing), which may include walking, without the conscious knowledge of the subject.
- Nocturia: A frequent need to get up and go to the bathroom to urinate at night. It differs from Enuresis, or bed-wetting, in which the person does not arouse from sleep, but the bladder nevertheless empties.
- Somniphobia: a dread of sleep.

Types

- Dyssomnias - A broad category of sleep disorders characterized by either hypersomnolence or insomnia. The three major subcategories include intrinsic (i.e., arising from within the body), extrinsic (secondary to environmental conditions or various pathologic conditions), and disturbances of circadian rhythm. MeSH
    - Insomnia
    - Narcolepsy
    - Sleep Disordered Breathing (SDB), including (non exhaustive):
        - Several types of Sleep apnea

        - Snoring
        - Upper airway resistance syndrome
    - Restless leg syndrome
    - Periodic limb movement disorder
    - Hypersomnia
        - Recurrent hypersomnia - including Kleine-Levin syndrome
        - Posttraumatic hypersomnia
        - "Healthy" hypersomnia
    - Circadian rhythm sleep disorders
        - Delayed sleep phase syndrome
        - Advanced sleep phase syndrome
        - Non-24-hour sleep-wake syndrome
- Parasomnias - A category of sleep disorders that involve abnormal and unnatural movements, behaviors, emotions, perceptions, and dreams in connection with sleep.
    - REM sleep behaviour disorder
    - Sleep terror
    - Sleepwalking (or somnambulism)
    - Bruxism (Tooth-grinding)
    - Bedwetting or sleep enuresis.
    - Sleep talking (or somniloquy)
    - Sleep sex (or sexsomnia)
    - Exploding head syndrome - Waking up in the night hearing loud noises.
- Medical or Psychiatric Conditions that may produce sleep disorders
    - Psychosis (such as Schizophrenia)
    - Mood disorders
        - Depression
        - Anxiety
    - Panic
    - Alcoholism
- Sleeping sickness - a parasitic disease which can be transmitted by the Tsetse fly.

General principles of treatment

Treatments for sleep disorders generally can be grouped into four categories:

- behavioral/ psychotherapeutic treatments
- rehabilitation/management
- medications
- other somatic treatments

None of these general approaches is sufficient for all patients with sleep disorders. Rather, the choice of a specific treatment depends on the patient's diagnosis, medical and psychiatric history, and preferences, as well as the expertise of the treating clinician. Often, behavioral/psychotherapeutic and pharmacological approaches are not incompatible and can effectively be combined to maximize therapeutic benefits.

Management of sleep disturbances that are secondary to mental, medical, or substance abuse disorders should focus on the underlying conditions.

Medications and somatic treatments may provide the most rapid symptomatic relief from some sleep disturbances. Some disorders, such as narcolepsy, are best treated pharmacologically. Others, such as chronic and primary insomnia, may be more amenable to behavioral interventions, with more durable results.

Chronic sleep disorders in childhood, which affect some 70% of children with developmental or psychological disorders, are under-reported and under-treated. Sleep-phase disruption is also common among adolescents, whose school schedules are often incompatible with their natural circadian rhythm. Effective treatment begins with careful diagnosis using sleep diaries and perhaps sleep studies. Modifications in sleep hygiene may resolve the problem, but medical treatment is often warranted.

Special equipment may be required for treatment of several disorders such as obstructive apnea, the circadian rhythm disorders and bruxism. In these cases, when severe, an acceptance of living with the disorder, however well managed, is often necessary.

Some sleep disorders have been found to compromise glucose metabolism.

Sleep medicine

Due to rapidly increasing knowledge about sleep in the 20th century, including the discovery of REM sleep and sleep apnea, the medical importance of sleep was recognized. The medical community began paying more attention than previously to primary sleep disorders, such as sleep apnea, as well as the role and quality of sleep in other conditions. By the 1970s in the USA, clinics and laboratories devoted to the study of sleep and sleep disorders had been founded, and a need for standards arose.

Sleep Medicine is now a recognized subspecialty within internal medicine, family medicine, pediatrics, otolaryngology, psychiatry and neurology in the United States. Certification in Sleep Medicine shows that the specialist:

"has demonstrated expertise in the diagnosis and management of clinical conditions that occur during sleep, that disturb sleep, or that are affected by disturbances in the wake-sleep cycle. This specialist is skilled in the analysis and interpretation of comprehensive polysomnography, and well-versed in emerging research and management of a sleep laboratory."

Competence in sleep medicine requires an understanding of a myriad of very diverse disorders, many of which present with similar symptoms such as excessive daytime sleepiness, which, in the absence of volitional sleep deprivation, "is almost inevitably caused by an identifiable and treatable sleep disorder", such as sleep apnea, narcolepsy, idiopathic central nervous system (CNS) hypersomnia, Kleine-Levin syndrome, menstrual-related hypersomnia, idiopathic recurrent stupor, or circadian rhythm

disturbances. Another common complaint is insomnia, a set of symptoms which can have a great many different causes, physical and mental. Management in the varying situations differs greatly and cannot be undertaken without a correct diagnosis.

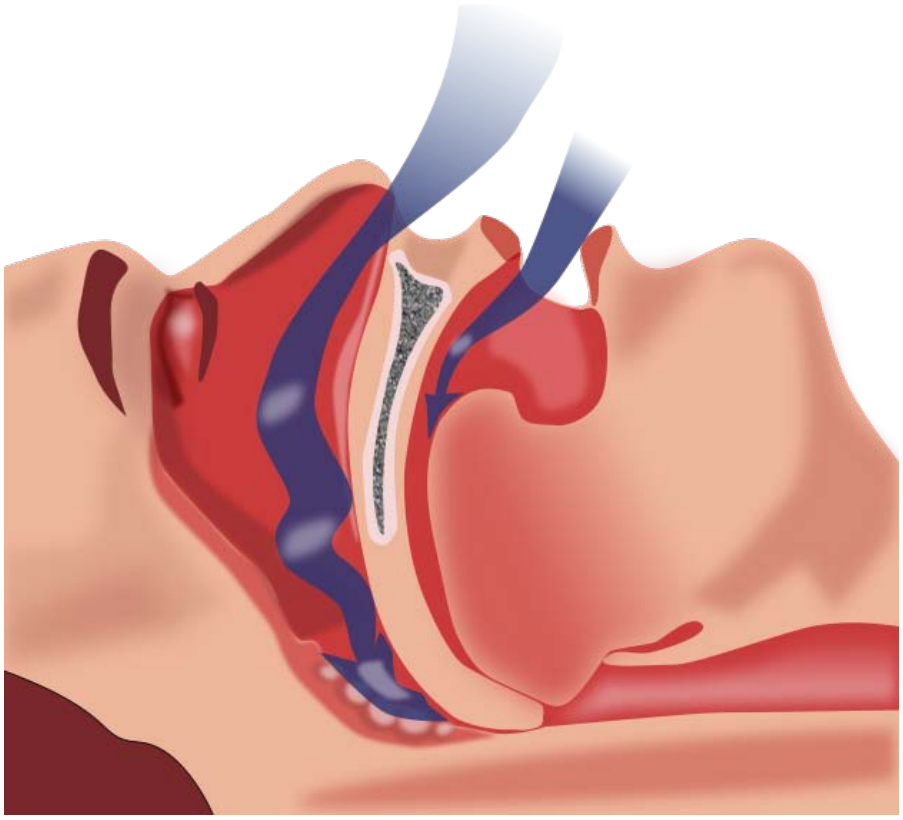
Sleep dentistry (bruxism, snoring and sleep apnea), while not recognized as one of the nine dental specialties, qualifies for board-certification by the American Board of Dental Sleep Medicine (ABDSM). The resulting Diplomate status is recognized by the American Academy of Sleep Medicine (AASM), and these dentists are organized in the Academy of Dental Sleep Medicine (USA). The qualified dentists collaborate with sleep physicians at accredited sleep centers and can provide oral appliance therapy and upper airway surgery to treat or manage sleep-related breathing disorders.

In the UK, knowledge of sleep medicine and possibilities for diagnosis and treatment seem to lag. Guardian.co.uk quotes the director of the Imperial College Healthcare Sleep Centre: "One problem is that there has been relatively little training in sleep medicine in this country – certainly there is no structured training for sleep physicians." The Imperial College Healthcare site shows attention to obstructive sleep apnea syndrome (OSA) and very few other sleep disorders.

Chapter 11

Sleep Apnea

Sleep apnea



Obstructive sleep apnea

ICD-10	G47.3
ICD-9	327.23, 780.57
eMedicine	ped/2114
MeSH	D012891

Sleep apnea (or **sleep apnoea** in British English) is a sleep disorder characterized by abnormal pauses in breathing or instances of abnormally low breathing, during sleep. Each pause in breathing, called an apnea, can last from a few seconds to minutes, and may occur 5 to 30 times or more an hour. Similarly, each abnormally low breathing event is called a hypopnea. Sleep apnea is diagnosed with an overnight sleep test called a polysomnogram, or "sleep study".

There are three forms of sleep apnea: central (CSA), obstructive (OSA), and complex or mixed sleep apnea (i.e., a combination of central and obstructive) constituting 0.4%, 84% and 15% of cases respectively. In CSA, breathing is interrupted by a lack of respiratory effort; in OSA, breathing is interrupted by a physical block to airflow despite respiratory effort, and snoring is common.

Regardless of type, an individual with sleep apnea is rarely aware of having difficulty breathing, even upon awakening. Sleep apnea is recognized as a problem by others witnessing the individual during episodes or is suspected because of its effects on the body (*sequelae*). Symptoms may be present for years (or even decades) without identification, during which time the sufferer may become conditioned to the daytime sleepiness and fatigue associated with significant levels of sleep disturbance.

Diagnosis

The diagnosis of Sleep Apnea is based on the conjoint evaluation of clinical symptoms (e.g. excessive daytime sleepiness and fatigue) and of the results of a formal sleep study (polysomnography, or reduced channels home based test). The latter aims at establishing an "objective" diagnosis indicator linked to the quantity of apneic events per hour of sleep (Apnea Hypnea Index(AHI), or Respiratory Disturbance Index (RDI)), associated to a formal threshold, above which a patient is considered as suffering from Sleep Apnea, and the severity of his sleep apnea can be then quantified. Nevertheless, due to the number and variability in the actual symptoms and nature of apneic events (hypopnea vs apnea, central vs. obstructive...), the variability of patients physiology, the intrinsic imperfections of the experimental setups and methods, this field is opened to debate. Within this context, the definition of an apneic event depends of several factors (e.g. patient's age) and account for this variability through a multi-criteria decision rule described in several, sometimes conflicting, guidelines. One example of a commonly adopted definition of an apnea (for an adult) includes a minimum 10 second interval between breaths, with either a neurological arousal (a 3-second or greater shift in EEG frequency, measured at C3, C4, O1, or O2) or a blood oxygen desaturation of 3–4% or greater, or both arousal and desaturation.

Classification

Obstructive sleep apnea

Obstructive sleep apnea (OSA) is the most common category of sleep-disordered breathing. The muscle tone of the body ordinarily relaxes during sleep, and at the level of

the throat the human airway is composed of collapsible walls of soft tissue which can obstruct breathing during sleep. Mild occasional sleep apnea, such as many people experience during an upper respiratory infection, may not be important, but chronic severe obstructive sleep apnea requires treatment to prevent low blood oxygen (hypoxemia), sleep deprivation, and other complication.

Individuals with low muscle tone and soft tissue around the airway (e.g., because of obesity) and structural features that give rise to a narrowed airway are at high risk for obstructive sleep apnea. The elderly are more likely to have OSA than young people. Men are more likely to suffer sleep apnea than women and children are, though it is not uncommon in the latter two population groups.

The risk of OSA rises with increasing body weight, active smoking and age. In addition, patients with diabetes or "borderline" diabetes have up to three times the risk of having OSA.

Common symptoms include loud snoring, restless sleep, and sleepiness during the daytime. Diagnostic tests include home oximetry or polysomnography in a sleep clinic.

Some treatments involve lifestyle changes, such as avoiding alcohol or muscle relaxants, losing weight, and quitting smoking. Many people benefit from sleeping at a 30-degree elevation of the upper body or higher, as if in a recliner. Doing so helps prevent the gravitational collapse of the airway. Lateral positions (sleeping on a side), as opposed to supine positions (sleeping on the back), are also recommended as a treatment for sleep apnea, largely because the gravitational component is smaller in the lateral position. Some people benefit from various kinds of oral appliances to keep the airway open during sleep. Continuous positive airway pressure (CPAP) is the treatment of choice . There are also surgical procedures to remove and tighten tissue and widen the airway.

As already mentioned, snoring is a common finding in people with this syndrome. Snoring is the turbulent sound of air moving through the back of the mouth, nose, and throat. Although not everyone who snores is experiencing difficulty breathing, snoring in combination with other conditions such as overweight and obesity has been found to be highly predictive of OSA risk. The loudness of the snoring is not indicative of the severity of obstruction, however. If the upper airways are tremendously obstructed, there may not be enough air movement to make much sound. Even the loudest snoring does not mean that an individual has sleep apnea syndrome. The sign that is most suggestive of sleep apneas occurs when snoring *stops*.

Other indicators include (but are not limited to): hypersomnolence, obesity BMI >30, large neck circumference (16 in (410 mm) in women, 17 in (430 mm) in men), enlarged tonsils and large tongue volume, micrognathia, morning headaches, irritability/mood-swings/depression, learning and/or memory difficulties, and sexual dysfunction.

The term "sleep-disordered breathing" is commonly used in the U.S. to describe the full range of breathing problems during sleep in which not enough air reaches the lungs

(hypopnea and apnea). Sleep-disordered breathing is associated with an increased risk of cardiovascular disease, stroke, high blood pressure, arrhythmias, diabetes, and sleep deprived driving accidents. When high blood pressure is caused by OSA, it is distinctive in that, unlike most cases of high blood pressure (so-called essential hypertension), the readings do *not* drop significantly when the individual is sleeping. Stroke is associated with obstructive sleep apnea.

In the June 27, 2008, edition of the journal *Neuroscience Letters*, researchers revealed that people with OSA show tissue loss in brain regions that help store memory, thus linking OSA with memory loss. Using magnetic resonance imaging (MRI), the scientists discovered that sleep apnea patients' mammillary bodies were nearly 20 percent smaller, particularly on the left side. One of the key investigators hypothesized that repeated drops in oxygen lead to the brain injury.

Central sleep apnea

In pure central sleep apnea or Cheyne-Stokes respiration, the brain's respiratory control centers are imbalanced during sleep. Blood levels of carbon dioxide, and the neurological feedback mechanism that monitors them, do not react quickly enough to maintain an even respiratory rate, with the entire system cycling between apnea and hyperpnea, even during wakefulness. The sleeper stops breathing and then starts again. There is no effort made to breathe during the pause in breathing: there are no chest movements and no struggling. After the episode of apnea, breathing may be faster (hyperpnea) for a period of time, a compensatory mechanism to blow off retained waste gases and absorb more oxygen.

While sleeping, a normal individual is "at rest" as far as cardiovascular workload is concerned. Breathing is regular in a healthy person during sleep, and oxygen levels and carbon dioxide levels in the bloodstream stay fairly constant. The respiratory drive is so strong that even conscious efforts to hold one's breath do not overcome it. Any sudden drop in oxygen or excess of carbon dioxide (even if tiny) strongly stimulates the brain's respiratory centers to breathe.

In central sleep apnea, the basic neurological controls for breathing rate malfunction and fail to give the signal to inhale, causing the individual to miss one or more cycles of breathing. If the pause in breathing is long enough, the percentage of oxygen in the circulation will drop to a lower than normal level (hypoxaemia) and the concentration of carbon dioxide will build to a higher than normal level (hypercapnia). In turn, these conditions of hypoxia and hypercapnia will trigger *additional* effects on the body. Brain cells need constant oxygen to live, and if the level of blood oxygen goes low enough for long enough, the consequences of brain damage and even death will occur. Fortunately, central sleep apnea is more often a chronic condition that causes much milder effects than sudden death. The exact effects of the condition will depend on how severe the apnea is and on the individual characteristics of the person having the apnea. Several examples are discussed below, and more about the nature of the condition is presented in the section on Clinical Details.

In any person, hypoxia and hypercapnia have certain common effects on the body. The heart rate will increase, unless there are such severe co-existing problems with the heart muscle itself or the autonomic nervous system that makes this compensatory increase impossible. The more translucent areas of the body will show a bluish or dusky cast from cyanosis, which is the change in hue that occurs owing to lack of oxygen in the blood ("turning blue"). Overdoses of drugs that are respiratory depressants (such as heroin, and other opiates) kill by damping the activity of the brain's respiratory control centers. In central sleep apnea, the effects of sleep *alone* can remove the brain's mandate for the body to breathe.

- Normal Respiratory Drive: After exhalation, the blood level of oxygen decreases and that of carbon dioxide increases. Exchange of gases with a lungful of fresh air is necessary to replenish oxygen and rid the bloodstream of built-up carbon dioxide. Oxygen and carbon dioxide receptors in the blood stream (called chemoreceptors) send nerve impulses to the brain, which then signals reflex opening of the larynx (so that the opening between the vocal cords enlarges) and movements of the rib cage muscles and diaphragm. These muscles expand the thorax (chest cavity) so that a partial vacuum is made within the lungs and air rushes in to fill it.
- Physiologic effects of central apnea: During central apneas, the central respiratory drive is absent, and the brain does *not* respond to changing blood levels of the respiratory gases. No breath is taken despite the normal signals to inhale. The immediate effects of central sleep apnea on the body depend on how long the failure to breathe endures. At worst, central sleep apnea may cause sudden death. Short of death, drops in blood oxygen may trigger seizures, even in the absence of epilepsy. In people *with* epilepsy, the hypoxia caused by apnea may trigger seizures that had previously been well controlled by medications. In other words, a seizure disorder may become unstable in the presence of sleep apnea. In adults with coronary artery disease, a severe drop in blood oxygen level can cause angina, arrhythmias, or heart attacks (myocardial infarction). Longstanding recurrent episodes of apnea, over months and years, may cause an increase in carbon dioxide levels that can change the pH of the blood enough to cause a metabolic acidosis.

Mixed apnea and complex sleep apnea

Some people with sleep apnea have a combination of both types. When obstructive sleep apnea syndrome is severe and longstanding, episodes of central apnea sometimes develop. The exact mechanism of the loss of central respiratory drive during sleep in OSA is unknown but is most commonly related to acid-base and CO_2 feedback malfunctions stemming from heart failure. There is a constellation of diseases and symptoms relating to body mass, cardiovascular, respiratory, and occasionally, neurological dysfunction that have a synergistic effect in sleep-disordered breathing. In some cases, a side effect from the lack of sleep is a mild case of Excessive Daytime Sleepiness (EDS) where the subject has had minimal sleep and this extreme fatigue over time takes its toll on the subject. The presence of central sleep apnea without an

obstructive component is a common result of chronic opiate use (or abuse) owing to the characteristic respiratory depression caused by large doses of narcotics.

Complex sleep apnea has recently been described by researchers as a novel presentation of sleep apnea. Patients with complex sleep apnea exhibit OSA, but upon application of positive airway pressure the patient exhibits persistent central sleep apnea. This central apnea is most commonly noted while on CPAP therapy after the obstructive component has been eliminated. This has long been seen in sleep laboratories and has historically been managed either by CPAP or BiLevel therapy. Adaptive servo-ventilation (ASV) modes of therapy have been introduced to attempt to manage this complex sleep apnea. Studies have demonstrated marginally superior performance of the adaptive servo ventilators in treating Cheyne-Stokes breathing; however, no longitudinal studies have yet been published, nor have any results been generated that suggest any differential outcomes versus standard CPAP therapy. At the AARC 2006 in Las Vegas, NV, researchers reported successful treatment of hundreds of patients on ASV therapy; however, these results have not been reported in peer-reviewed publications as of July 2007.

An important finding by Dernaika et al. suggests that transient central apnea produced during CPAP titration (the so-called "complex sleep apnea") is "…transient and self-limited." The central apneas may in fact be secondary to sleep fragmentation during the titration process. As of July 2007, there has been no alternate convincing evidence produced that these central sleep apnea events associated with CPAP therapy for obstructive sleep apnea are of any significant pathophysiologic importance.

Research is ongoing, however, at the Harvard Medical School, including adding dead space to positive airway pressure for treatment of complex sleep-disordered breathing.

Treatment

For mild cases of sleep apnea, a treatment which is a lifestyle change is sleeping on one's side, which can prevent the tongue and palate from falling backwards in the throat and blocking the airway. Another is avoiding alcohol and sleeping pills, which can relax throat muscles, contributing to the collapse of the airway at night.

For moderate to severe sleep apnea, the most common treatment is the use of a continuous positive airway pressure (CPAP) device, which 'splints' the patient's airway open during sleep by means of a flow of pressurized air into the throat. The patient typically wears a plastic facial mask, which is connected by a flexible tube to a small bedside CPAP machine. The CPAP machine generates the required air pressure to keep the patient's airways open during sleep. Advanced models may warm or humidify the air and monitor the patient's breathing to ensure proper treatment. Although CPAP therapy is extremely effective in reducing apneas and less expensive than other treatments, some patients find it extremely uncomfortable. Many patients refuse to continue the therapy or fail to use their CPAP machines on a nightly basis.

In addition to CPAP, dentists specializing in sleep disorders can prescribe Oral Appliance Therapy (OAT). The oral appliance is a custom-made mouthpiece that shifts the lower jaw forward, opening up the airway. OAT is usually successful in patients with mild to moderate obstructive sleep apnea. OAT is a relatively new treatment option for sleep apnea in the United States, but it is much more common in Canada and Europe.

Several levels of obstruction may be addressed in physical treatment, including the nasal passage, throat (pharynx), base of tongue, and facial skeleton. Surgical treatment for obstructive sleep apnea needs to be individualized in order to address all anatomical areas of obstruction. Often, correction of the nasal passages needs to be performed in addition to correction of the oropharynx passage. Septoplasty and turbinate surgery may improve the nasal airway. Tonsillectomy and uvulopalatopharyngoplasty (UPPP or UP3) are available to address pharyngeal obstruction. Base-of-tongue advancement by means of advancing the genial tubercle of the mandible may help with the lower pharynx. A myriad of other techniques are available, including hyoid bone myotomy and suspension and various radiofrequency technologies.

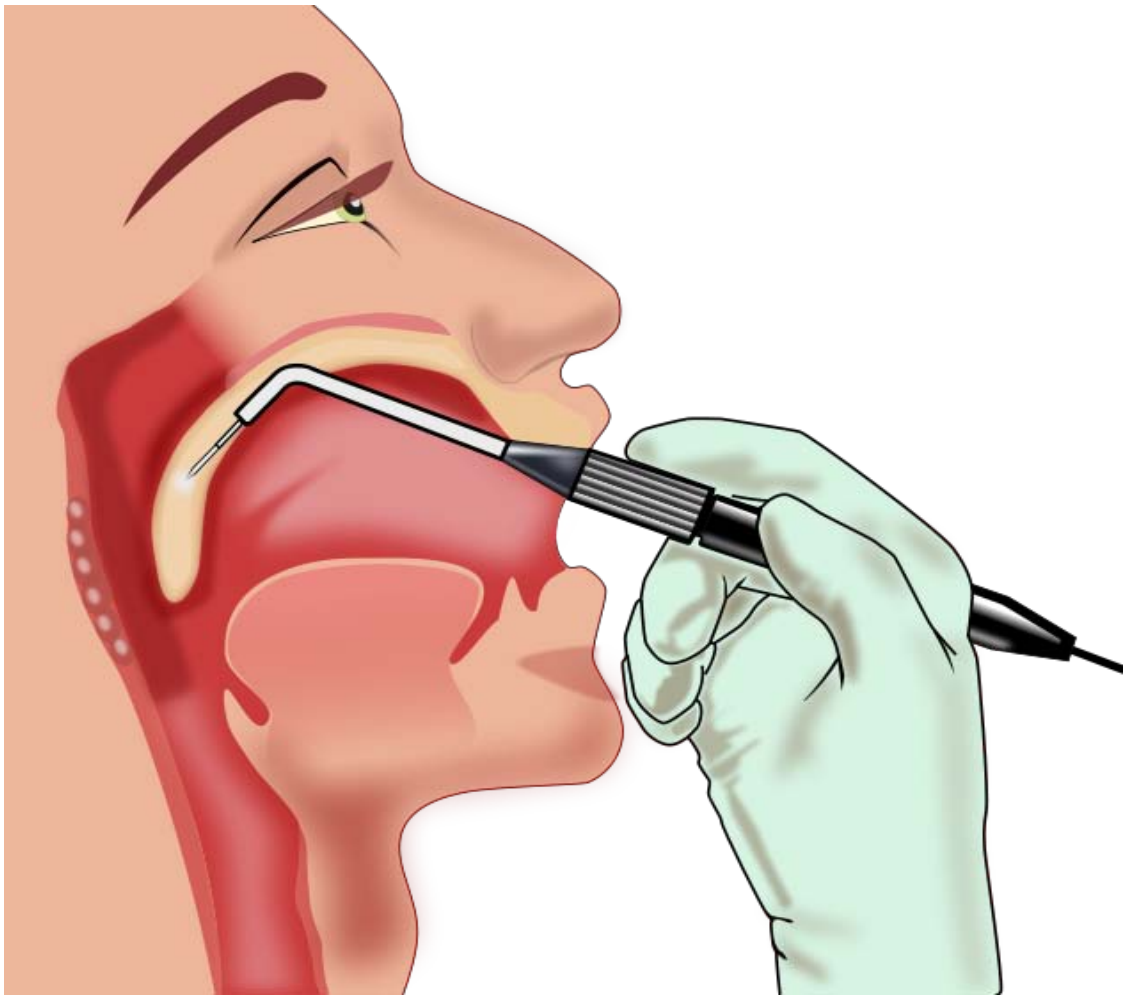


Illustration of surgery on the mouth and throat

Other surgery options may attempt to shrink or stiffen excess tissue in the mouth or throat, procedures done at either a doctor's office or a hospital. Small shots or other treatments, sometimes in a series, are used for shrinkage, while the insertion of a small piece of stiff plastic is used in the case of surgery whose goal is to stiffen tissues.

Possibly owing to changes in pulmonary oxygen stores, sleeping on one's side (as opposed to on one's back) has been found to be helpful for central sleep apnea with Cheyne-Stokes respiration (CSA-CSR).

Medications like Acetazolamide lower blood pH and encourage respiration. Low doses of oxygen are also used as a treatment for hypoxia but are discouraged due to side effects.

Surgery

CPAP is the most consistently safe and effective treatment for obstructive sleep apnea but it is not a cure, and people are less likely to use it in the long term. The Stanford Center for Excellence in Sleep Disorders Medicine achieved a 95% cure rate of sleep apnea patients by surgery. Maxillomandibular advancement (MMA) is considered the most effective surgery for sleep apnea patients, because it increases the posterior airway space (PAS). The main benefit of the operation is that the oxygen saturation in the arterial blood increases. In a study published in 2008, 93.3.% of surgery patients achieved an adequate quality of life based on the Functional Outcomes of Sleep Questionnaire (FOSQ). Surgery led to a significant increase in general productivity, social outcome, activity level, vigilance, intimacy and sex, and the total score postoperatively was P = .0002. Overall risks of MMA surgery are low: The Stanford University Sleep Disorders Center found 4 failures in a series of 177 patients, or about one out of 44 patients.

Several inpatient and outpatient procedures use sedation. Many drugs and agents used during surgery to relieve pain and to depress consciousness remain in the body at low amounts for hours or even days afterwards. In an individual with either central, obstructive or mixed sleep apnea, these low doses may be enough to cause life-threatening irregularities in breathing or collapses in a patient’s airways. Use of analgesics and sedatives in these patients postoperatively should therefore be minimized or avoided.

Surgery on the mouth and throat, as well as dental surgery and procedures, can result in postoperative swelling of the lining of the mouth and other areas that affect the airway. Even when the surgical procedure is designed to improve the airway, such as tonsillectomy and adenoidectomy or tongue reduction, swelling may negate some of the effects in the immediate postoperative period. Once the swelling resolves and the palate becomes tightened by postoperative scarring, however, the full benefit of the surgery may be noticed.

Sleep apnea patients undergoing any medical treatment must make sure his or her doctor and/or anesthetist are informed about their condition. Alternate and emergency procedures may be necessary to maintain the airway of sleep apnea patients. If an

individual suspects he or she may have sleep apnea, communication with their doctor about possible preprocedure screening may be in order.

Alternative treatments

A 2005 study in the British Medical Journal found that learning and practicing the didgeridoo helped reduce snoring and sleep apnea as well as daytime sleepiness. This appears to work by strengthening muscles in the upper airway, thus reducing their tendency to collapse during sleep.

A 2009 study published in the American Journal of Respiratory and Clinical Care Medicine found that "oropharyngeal exercises derived from speech therapy may be an effective treatment option for patients with moderate" obstructive sleep apnea .

Epidemiology

The Wisconsin Sleep Cohort Study estimated in 1993 that roughly one in every 15 Americans were affected by at least moderate sleep apnea. It also estimated that in middle-age as many as nine percent of women and 24 percent of men were affected, undiagnosed and untreated.

The costs of untreated sleep apnea reach further than just health issues. It is estimated that in the U.S. the average untreated sleep apnea patient's annual health care costs $1,336 more than an individual without sleep apnea. This may cause $3.4 billion/year in additional medical costs. Whether medical cost savings occur with treatment of sleep apnea remains to be determined.

History

The clinical picture of this condition has long been recognized as a character trait, without an understanding of the disease process. The term "Pickwickian syndrome" that is sometimes used for the syndrome was coined by the famous early 20th century physician, William Osler, who must have been a reader of Charles Dickens. The description of Joe, "the fat boy" in Dickens's novel *The Pickwick Papers*, is an accurate clinical picture of an adult with obstructive sleep apnea syndrome.

The early reports of obstructive sleep apnea in the medical literature described individuals who were very severely affected, often presenting with severe hypoxemia, hypercapnia and congestive heart failure.

The management of obstructive sleep apnea was revolutionized with the introduction of continuous positive airway pressure (CPAP), first described in 1981 by Colin Sullivan and associates in Sydney, Australia. The first models were bulky and noisy, but the design was rapidly improved and by the late 1980s CPAP was widely adopted. The availability of an effective treatment stimulated an aggressive search for affected individuals and led to the establishment of hundreds of specialized clinics dedicated to

the diagnosis and treatment of sleep disorders. Though many types of sleep problems are recognized, the vast majority of patients attending these centers have sleep-disordered breathing.

Chapter 12

Hypopnea

Hypopnea (sometimes spelled **hypopnœa**) is a medical term for a disorder which involves episodes of overly shallow breathing or an abnormally low respiratory rate. This differs from apnea in that there remains some flow of air. Hypopnea events may happen while asleep or while awake.

During sleep, hypopnea is classed as a sleep disorder. With moderate to severe hypopnea, sleep is disturbed such that patients may get a full night's sleep but still not feel rested because they did not get the right kind of sleep. The disruption in breathing causes a drop in blood oxygen level, which may in turn disrupt the stages of sleep.

Daytime hypopnea events are mostly limited to those with severely compromised respiratory muscles, as occurs in certain neuromuscular diseases. Similarly, daytime hypopnea can also cause a drop in blood oxygen level.

Etymology

Hypopnea comes from the Greek roots *hypo-* (meaning *low*, *under*, *beneath*, *down*, *below normal*) and *pnoe* (meaning *breathing*). Literally it means underbreathing.

General information

In the context of diagnosis and treatment of sleep disorders, a hypopnea event is not considered to be clinically significant unless there is a 30% (or greater) reduction in flow lasting for 10 seconds or longer and an associated 4% (or greater) desaturation in the person's O_2 levels, or if it results in arousal or fragmentation of sleep.

The direct consequence of hypopnea (as well as apnea) is that the CO_2 in the blood increases and the oxygen level in the patient’s blood decrease is proportionate to the severity of the airway obstruction. This disruptive pattern of breathing generates disruptive sleep patterns, the consequences of which being that those individuals may exhibit increased fatiguability, lethargy, decreased ability to concentrate, increased irritability, and morning headaches. Basically, those individuals are extremely tired due to their inability to get a good night’s sleep.

Hypopneas can be either central (i.e., as part of a waxing and waning in breathing effort) or obstructive in origin. During an obstructive hypopnea, in comparison to an obstructive apnea, the airway is only partially closed. However, this closure is still enough to cause a physiological effect (i.e., an oxygen desaturation and/or an increase in breathing effort terminating in arousal).

A hypopnea index (HI) can be calculated by dividing the number of hypopnea events during the sleep period by the number of hours of sleep. The apnea-hypopnea index (AHI) is an index of severity that combines apneas and hypopneas. Combining them both gives an overall severity of sleep apnea including sleep disruptions and desaturations (a low level of oxygen in the blood). The apnea-hypopnea index, like the apnea index and hypopnea index, is calculated by dividing the number of apneas and hypopneas by the number of hours of sleep. Another index that is used to measure sleep apnea is the respiratory disturbance index (RDI). The respiratory disturbance index is similar to the apnea-hypopnea index; however, it also includes respiratory events that do not technically meet the definitions of apneas or hypopneas, but do disrupt sleep.

Causes

Among the causes of hypopnea are:

- anatomical defects such as nasal septum deformation or congenital narrowness of nasal meati and the gullet;
- acute tonsillitis and/or adenoiditis;
- obesity or being overweight;
- neuromuscular disease or any condition that entails weakened respiratory muscles;
- use of sedatives (sleeping pills, etc.);
- alcohol abuse;
- smoking;
- aging;
- others;

most of which are also typical causes of airway obstruction, snoring and sleep apnea.

Symptoms

The most common hypopnea symptom is excessive sleepiness, which results from constant sleep interruption. People with hypopnea often have loud, heavy snoring that is interrupted with choking sounds or loud snorts followed by periods of silence, because not enough air can flow into the lungs through the mouth and nose. The periods of silence can last 20 seconds or longer and can happen many times each hour, resulting in poor sleep and reduced levels of oxygen in the blood.

Other symptoms of hypopnea may include depression, forgetfulness, mood or behavior changes, trouble concentrating, loss of energy, nervousness, and morning headaches. Not

all people with hypopnea experience all of these symptoms and not everyone who has these symptoms has hypopnea.

Consequences

Hypopnea is a disorder that may result in excessive daytime sleepiness and compromised quality of life, including traffic accidents, diminished productivity in the work place and emotional problems.

Cardiovascular consequences of hypopnea may include myocardial infarction, stroke, psychiatric problems, impotence, cognitive dysfunction, hypertension, coronary heart disease, and memory loss.

Treatment

The most common treatment for hypopnea is continuous positive airway pressure (CPAP). CPAP is a treatment in which the patient wears a mask over the nose and/or mouth. An air blower forces air through the upper airway. The air pressure is adjusted so that it is just enough to maintain the oxygen saturation levels in the blood. For people with neuromuscular disorders, the most common treatment is the use of BIPAP or other non-invasive ventilation.

Mild hypopnea can often be treated by losing weight or by avoiding sleeping on one's back. Also quitting smoking, and avoiding alcohol, sedatives and hypnotics (soporifics) before sleep can be quite effective.

Surgery is generally a last resort in hypopnea treatment, but is a site-specific option for the upper airway. Depending on the cause of obstruction, surgery may focus on the soft palate, the uvula, tonsils, adenoids or the tongue. There are also more complex surgeries that are performed with the adjustment of other bone structures - the mouth, nose and facial bones.

Chapter 13

Parasomnia

Parasomnia	
ICD-10	F51.3-F51.4
ICD-9	307.47, 327.4, 780.59
eMedicine	med/3131
MeSH	D020447

Parasomnias are a category of sleep disorders that involve abnormal and unnatural movements, behaviors, emotions, perceptions, and dreams that occur while falling asleep, sleeping, between sleep stages, or during arousal from sleep. Most parasomnias are dissociated sleep states which are partial arousals during the transitions between wakefulness and NREM sleep, or wakefulness and REM sleep.

NREM parasomnias

NREM parasomnias are arousal disorders that occur during stage 3 (or 4 by the R&K standardization) of NREM sleep—also known as slow wave sleep (SWS). They are caused by a physiological activation in which the patient's brain exits from SWS and is caught in between a sleeping and waking state. In particular, these disorders involve activation of the autonomic nervous system, motor system, or cognitive processes during sleep or sleep-wake transitions.

Some NREM parasomnias are common during childhood but decrease in frequency with increasing age (sleep-walking, night-terrors, and confusional arousal). They can be triggered in certain individuals by alcohol, sleep deprivation, physical activity, emotional stress, depression, medications, or a fevered illness. These disorders of arousal can range from confusional arousals, somnambulism, to night terrors. Other specific disorders include sleepeating, sleep sex, teeth grinding, rhythmic movement disorder, restless legs syndrome, and somniloquy.

Confusional arousals

With a prevalence of 4%, confusional arousals are not observed very often in adults; however, they are common in children. Confusional arousals are occasional thrashings or inconsolable crying among children—they are characterized by movements in bed.

Sleepwalking (somnambulism)

Sleepwalking has a prevalence of 1-17% in childhood, with the most frequent occurrences around the age of eleven-twelve. About 4% of adults experience somnambulism.

Sleep terrors (night terrors)

Sleep terrors is the most disruptive arousal disorder since it may involve loud screams and panic; in extreme cases, it may result in bodily harm or property damage by running about or hitting walls. Unfortunately, all attempts to console the individual are futile and may prolong or intensify the victim's confused state. Usually the victim experiences amnesia after the event but it may not be complete amnesia. Up to 3% of adults suffer from sleep terrors, and exhibited behavior of this parasomnia can range from mild to extremely violent. They typically occur in stages 3 and 4 sleep.

Bruxism (teeth grinding)

Bruxism is a common sleep disorder where the sufferer grinds their teeth during sleep. This can cause sleep disruption for the sufferer and bed partner, wear and fracture of teeth, and jaw pain.

Restless legs syndrome & Periodic Limb Movements

Both of these conditions (RLS and PLM) are classified as dyssomnias according to the DSM-IV. They are considered parasomnias.

REM parasomnias

REM sleep behavior disorder

REM Sleep Behavior Disorder is the most common REM sleep parasomnia in which muscle atonia is absent. This allows the individual to act out their dreams and may result in repeated injury-- bruises, lacerations and fractures-- to themselves or others. Patients may take self-protection measures by tethering themselves to bed, using pillow barricades or sleeping in an empty room on a mattress. Demographically, 90% of RBD patients are males, and most are older than 50 years of age.

Typical clinical features of REM sleep behaviour disorder are:

- Male gender predeliction
- Mean age of onset 50–65 years (range 20–80 years)
- Vocalisation, screaming, swearing that may be associated with dreams
- Motor activity, simple or complex, that may result in injury to patient or bed-partner
- Occurrence usually in latter half of sleep period (REM sleep)
- May be associated with neurodegenerative disease

Acute RBD, occurs mostly as a result of a side-effect in prescribed medication- usually antidepressants.

Chronic RBD is idiopathic or associated with neurological disorders. There is a growing association of chronic RBD with neurodegenerative disorders – Parkinson's disease, multiple system atrophy (MSA) or dementia-- as an early indicator of these conditions by as much as 10 years.

Patients with narcolepsy also are more likely to develop RBD.

Catathrenia

Catathrenia, a rapid eye movement sleep parasomnia consisting of breath holding and expiratory groaning during sleep, is distinct from both somniloquy and obstructive sleep apnea. The sound is produced during exhalation as opposed to snoring which occurs during inhalation. It is usually not noticed by the person producing the sound but can be extremely disturbing to sleep partners, although once aware of it, sufferers tend to be woken up by their own groaning as well. Bed partners generally report hearing the person take a deep breath, hold it, then slowly exhale; often with a high-pitched squeak or groaning sound.

Chapter 14

Rapid Eye Movement Behavior Disorder and Sleepwalking

Rapid eye movement behavior disorder

Rapid eye movement sleep behavior disorder

MeSH D020447

Rapid eye movement sleep behavior disorder (**RBD**) is a sleep disorder (more specifically a parasomnia) that involves abnormal behavior during the sleep phase with rapid eye movement (REM sleep). It was first described in 1986.

The major and arguably only abnormal feature of RBD is loss of muscle atonia (paralysis) during otherwise intact REM sleep. This is the stage of sleep in which most vivid dreaming occurs. The loss of motor inhibition leads to a wide spectrum of behavioral release during sleep. This extends from simple limb twitches to more complex integrated movement, in which sufferers appear to be unconsciously acting out their dreams. These behaviors can be violent in nature and in some cases will result in injury to either the patient or their bed partner.

Symptoms

RBD is characterized by the dreamer acting out his or her dreams. Usually negative ones which involve kicking, screaming, punching, grabbing, and even jumping out of bed. When awakened, one can usually recall the dream they were having which will match the actions they were performing, but they will not be aware that they were moving. Episodes occur more towards the morning hours because that is when REM sleep is more frequent. People with RBD experience episodes at least once a week, sometimes more and each episode can result in injuries to oneself or one's bed partner.

Causes

Rapid eye movement behavior disorder occurs when there is a loss of normal voluntary muscle atonia during REM sleep resulting in motor behavior in response to dream content. It can be caused by adverse reactions to certain drugs or else during drug withdrawal; however it is most often associated with the elderly and in those with neurodegenerative disorders such as Parkinson disease, and other neurodegenerative diseases for example multiple system atrophy and Lewy Body Dementia.

Treatment

RBD is treatable. Various medications are prescribed for RBD based on varying symptoms. Low doses of clonazepam is most effective with a 90% success rate, how this drug works to restore REM atonia is unclear, however it is thought to suppress muscle activity, rather than directly restoring atonia. Melatonin is also effective and can also be prescribed as a more natural alternative. For those with Parkinson's and RBD, Levodopa is a popular choice. Pramipexole is another drug which can be an effective treatment option.

In addition to medication it is also wise to secure the sleeper's environment in preparation for episodes. Remove potentially dangerous objects from the bedroom and either place a cushion around the bed or move the mattress to the floor for added protect against injuries.

Epidemiology

The most comprehensive assessment so far has estimated RBD prevalence to be around 0.5% in individuals aged 15 to 100. It is far more common in males: most studies report that only around a tenth of sufferers are female. This may partially be due to a referral bias, as violent activity carried out by men is more likely to result in harm and injury and is more likely to be reported than injury to male bed partners by women, or it may reflect a true difference in prevalence as a result of genetic or androgenic factors. The mean age of onset is estimated to be around 60 years.

Various conditions are very similar to RBD in that sufferers exhibit excessive sleep movement and potentially violent behavior. Such disorders include sleepwalking and sleep terrors, which are associated with other stages of sleep, nocturnal seizures and obstructive sleep apnea which can induce arousals from REM sleep associated with complex behaviors. Because of the similarities between the conditions, polysomnography plays an important role in confirming RBD diagnosis.

It is now apparent that RBD appears in association with a variety of different conditions. Narcolepsy has been reported as a related disorder. Both RBD and narcolepsy involve dissociation of sleep states probably arising from a disruption of sleep control mechanisms. RBD has also been reported following cerebrovascular accident and neurinoma (tumour), indicating that damage to the brain stem area may precipitate RBD.

RBD is usually chronic, however may be acute and sudden in onset if associated with drug treatment or withdrawal (particularly with alcohol withdrawal) 60% of RBD is idiopathic. This includes RBD that is found in association with conditions such as Parkinson's disease and dementia with Lewy bodies, where it is often seen to precede the onset of neurodegenerative disease. RBD has been associated with autism. Monoamine oxidase inhibitors, tricyclic antidepressants, serotonergic synaptic reuptake inhibitors, and noradrenergic antagonists can induce or aggravate RBD symptoms and should be avoided in patients with RBD.

In non-humans

RBD has been diagnosed in non-humans, specifically, dogs.

Sleepwalking

Sleepwalking	
ICD-10	F51.3

Sleepwalking as seen by a Somalian artist

Sleepwalking, also known as **somnambulism**, is a sleep disorder belonging to the parasomnia family. Sleepwalkers arise from the slow wave sleep stage in a state of low consciousness and perform activities that are usually performed during a state of full consciousness. These activities can be as benign as sitting up in bed, walking to the bathroom, and cleaning, or as hazardous as cooking, driving, extremely violent gestures, grabbing at hallucinated objects, or even homicide.

Although generally sleepwalking cases consist of simple, repeated behaviours, there are occasionally reports of people performing complex behaviours while asleep, although their legitimacy is often disputed. In 2004, sleep medicine experts in Australia claimed to have successfully treated a woman who claimed to have sex with strangers in her sleep.

In December 2008, reports were published of a woman who sent semi-coherent emails while sleepwalking, including one inviting a friend around for dinner and drinks. Sleepwalkers often have little or no memory of the incident, as they are not truly conscious. Although their eyes are open, their expression is dim and glazed over. Sleepwalking may last as little as 30 seconds or as long as 30 minutes.

Nomenclature, classification, and codification

According to a study by Dr. Christina A. Gurnett, of the Washington University School of Medicine's Department of Neurology, sleepwalking was inherited as an autosomal dominant disorder with reduced penetrance in this family. Genome-wide multipoint parametric linkage analysis for sleepwalking revealed a maximum logarithm of the odds score of 3.44 at chromosome 20q12-q13.12 between 55.6 and 61.4 cM.

Explanation

Sleep stages

Sleep is categorized into stages of a cycle between REM sleep and NREM sleep. NREM sleep is further divided into four stages: stage 1 (a light sleep period), stage 2 (a consolidated sleep period), and stage 3 and 4 (slow wave sleep periods). This is followed by stage 3, stage 2, stage 1, and a REM period. In normal adults, a cycle will last about 1.5 hours. According to Lavie, Malhotra, and Pillar, "The length and content of sleep cycles change throughout the night as well as with age." Sleepwalking generally occurs during the first third of the night (between 11 p.m. and 1 a.m.) during the slow wave NREM sleep stage. High delta activity within the brain usually accompanies slow wave NREM sleep, and when 20–50% of all activity is delta activity, stage 3 is scored. When delta activity reaches 50% or higher, stage 4 is scored. Usually, if sleepwalking occurs at all, it will only occur once in a night.

Automatism

Researchers sometimes disagree about the classification of sleepwalking as an automatism. According to the popular source of MedicineNet, an automatism is "an unconscious movement that may resemble simple repetitive tics or may be a complex sequence of natural-looking movements." The individual often won't remember what he was doing or how he was doing it. These repetitive actions may include chewing, lip-smacking, pulling at clothing, or wandering around looking confused. Epileptic automatisms are also associated "with the absence attacks of petit mal epilepsy." In the case of the law, an individual can be accused of non-insane automatism or insane automatism. The first is used as a defense for temporary insanity or involuntary conduct, resulting in acquittal. The latter results in a "special verdict of not guilty by reason of insanity." This verdict of insanity can result in a court order to attend a mental institution. Some actions that take place during sleepwalking could be classified as automatisms.

Causes

Several experts theorize that the development of sleepwalking in childhood is due to a delay in maturation. There are also high-voltage delta waves in somnambulists up to 17 years of age. This presence might suggest an immaturity in the central nervous system, also a possible cause of sleepwalking. Sleepwalking is clustered in families, and the percentage of childhood sleepwalking increases to 45% if one parent was affected, and 60% if both parents were affected. However, there is no recorded preference to male or female individuals. Thus, heritable factors appear to predispose an individual to develop sleepwalking, but expression of the trait may be also influenced by environmental factors. Other precipitating factors to sleepwalking are those factors which increase the slow wave sleep stage. These most commonly include sleep deprivation, fever, and excessive tiredness. The use of some neuroleptics or hypnotics can also cause sleepwalking to occur.

Treatment

There are some drugs that can be prescribed for sleepwalkers such as a low dose benzodiazepine, tricyclic antidepressants, and clonazepam. However, for most sleepwalkers, many experts advise putting away dangerous items and locking doors and windows before sleep to reduce risks of harmful activity. Good sleep hygiene and avoiding sleep deprivation is also recommended.

There are conflicting viewpoints on whether it is harmful to wake a sleepwalker. Some experts say that sleepwalkers should be gently guided back to bed without waking them. Others counter that idea and state that waking a sleepwalker may result in their disorientation, but it is not harmful.

Epidemiology

According to the National Sleep Foundation, sleepwalking is prevalent in 1–15% of the general populace. Sleepwalking is most prevalent in children, and usually disappears by adolescence. Sleepwalking in adults is less common, but when it does occur, the events occur three times more often per year and last for more years than in children. Sleepwalking in old age is rare and usually indicates another disorder. Old age disorders may include delirium, drug toxicity or a seizure disorder.

Children

Sleepwalking events are common in childhood and decrease with age. According to Lavie, Malhotra and Pillar, the peak age is 4–8 years, when prevalence is 20% frequency of events. It is also known that "between 25–33% of somnambulists have nocturnal enuresis" (bed-wetting). Like sleepwalking, enuresis is more common in children and fades away as the child ages. Some children who sleepwalk are also affected by night terrors. However, night terrors are much more common in adult sleepwalkers, up to 50% more common. Some parents worry about the psychological implications of sleepwalking

on their child, but Larissa Hirsch, MD, editor of the website KidsHealth, says, "Sleepwalking is not usually a sign that something is emotionally or psychologically wrong with a child. And it doesn't cause any emotional harm."

In the study "sleepwalking and sleep terrors in prepubera children" they found that if a child had another sleepdisorder such as restless leg syndrome (RLS) or sleep-disorder breathing (SDB) that they had a greater chance of sleepwalking. The study found children with chronic parasomnias may often also present SDB or, to a lesser extent, RLS. Furthermore, the disappearance of the parasomnias after the treatment of the SDB or RLS periodic limb movement syndrome suggests that the latter may trigger the former. The high frequency of SDB in family members of children with parasomnia provided additional evidence that SDB may manifest as parasomnias in children. Children with parasomnias are not systematically monitored during sleep, although past studies have suggested that patients with sleep terrors or sleepwalking have an elevated level of brief EEG arousals. When children receive polysomnographies, discrete patterns (e.g., nasal flow limitation, abnormal respiratory effort, bursts of high or slow EEG frequencies) should be sought; apneas are rarely found in children. Children's respiration during sleep should be monitored with nasal cannula/pressure transducer system and/or esophageal manometry, which are more sensitive than the thermistors or thermocouples currently used in many laboratories. The clear, prompt improvement of severe parasomnia in children who are treated for SDB, as defined here, provides important evidence that subtle SDB can have substantial health-related significance. Also noteworthy is the report of familial presence of parasomnia. Studies of twin cohorts and families with sleep terror and sleepwalking suggest genetic involvement of parasomnias. RLS and SDB have been shown to have familial recurrence. RLS has been shown to have genetic involvement.

Adults

The persistence or onset of sleepwalking in adulthood is far less common than in children. It is a misconception that adult sleepwalking always indicates a psychological disorder. Sleepwalking can, however, be a symptom of people with psychological disorders. In one study, adult test subjects were given the Minnesota Multiphasic Personality Inventory, a psychiatric test. According to the study, patients showed "outwardly directed behavior patterns...suggest[ing] that these adults had difficulty handling aggression. They did not support an interpretation of sleepwalking as 'hysterical dissociation'."

Psychological disorders and drug use

In some cases, sleepwalking in adults may be a symptom of a psychological disorder or of drug use. One study done by A.H. Crisp et al. of St. George's Hospital Medical School in London supports the possibility of dissociation in adult sleepwalkers because the test subjects scored unusually high on the hysteria portion of the Crown-Crisp experiential index. According to J.E. Orme, an expert in psychology, "A higher incidence [of sleepwalking events] has been reported in patients with schizophrenia, hysteria and anxiety neuroses." Also, patients with migraine headaches or Tourette Syndrome are 4–6

times more likely to sleepwalk. Some medications that may increase sleepwalking include: Chlorpromazine (Thorazine), perphenazine (Trilafon), lithium, benzodiazepine (Triazolam), amitriptylin (Elavel, Endep), Zolpidem (Ambien) and beta blockers.

History

Sleepwalking has attracted a sense of mystery, but it had not been seriously investigated and diagnosed until the last century. Sleepwalking was initially thought to be a dreamer acting out a dream. For example, in one study published by the Society for Science & the Public in 1954, this was the conclusion: "Repression of hostile feelings against the father caused the patients to react by acting out in a dream world with sleepwalking, the distorted fantasies they had about all authoritarian figures, such as fathers, officers and stern superiors." This same group published an article twelve years later with a new conclusion: "Sleepwalking, contrary to most belief, apparently has little to do with dreaming. In fact, it occurs when the sleeper is enjoying his most oblivious, deepest sleep—a stage in which dreams are not usually reported." More recent research has discovered that sleepwalking is actually a disorder of NREM (non-rapid eye movement) arousal. Acting out a dream is the basis for a REM (rapid eye movement) sleep disorder called REM Behavior Disorder (or REM Sleep Behavior Disorder, RSBD). More accurate data about sleep is due to the invention of technologies such as the electroencephalogram (EEG) by Hans Berger in 1924 and BEAM by Frank Duffy in the early 1980s.

Chapter 15

Delayed Sleep Phase Syndrome

Delayed sleep phase syndrome	
ICD-10	G47.2
ICD-9	327.31
eMedicine	neuro/655
MeSH	D021081

Delayed sleep-phase syndrome (DSPS), also known as **delayed sleep-phase disorder** (DSPD) or **delayed sleep-phase type** (DSPT), is a circadian rhythm sleep disorder, a chronic disorder of the timing of sleep, peak period of alertness, the core body temperature rhythm, hormonal and other daily rhythms, compared to the normal population and relative to societal requirements. People with DSPS generally fall asleep some hours after midnight and have difficulty waking up in the morning.

Often, people with the disorder report that they cannot sleep until early morning, but fall asleep at about the same time every "night". Unless they have another sleep disorder such as sleep apnea in addition to DSPS, patients can sleep well and have a normal need for sleep. Therefore, they find it very difficult to wake up in time for a typical school or work day. If, however, they are allowed to follow their own schedules, e.g. sleeping from 4 a.m. to noon, they sleep soundly, awaken spontaneously, and do not experience excessive daytime sleepiness.

The syndrome usually develops in early childhood or adolescence. An adolescent version disappears in adolescence or early adulthood; otherwise DSPS is a lifelong condition. Depending on the severity, it can be to a greater or lesser degree treatable. Prevalence among adults, equally distributed among women and men, is approximately 0.15%, or 3 in 2,000.

DSPS was first formally described in 1981 by Dr. Elliot D. Weitzman and others at Montefiore Medical Center. It is responsible for 7–10% of patient complaints of chronic insomnia. However, as few doctors are aware of it, it often goes untreated or is treated inappropriately; DSPS is often misdiagnosed as primary insomnia or as a psychiatric condition. At its most severe and inflexible, it is an invisible disability.

Definition

According to the International Classification of Sleep Disorders (ICSD), the circadian rhythm sleep disorders share a common underlying chronophysiologic basis:

The major feature of these disorders is a misalignment between the patient's sleep pattern and the sleep pattern that is desired or regarded as the societal norm... In most circadian rhythm sleep disorders, the underlying problem is that the patient cannot sleep when sleep is desired, needed or expected.

The ICSD (page 128-133) diagnostic criteria for delayed sleep-phase syndrome are:

1. There is an intractable delay in the phase of the major sleep period in relation to the desired clock time, as evidenced by a chronic or recurrent complaint of inability to fall asleep at a desired conventional clock time together with the inability to awaken at a desired and socially acceptable time.
2. When not required to maintain a strict schedule, patients will exhibit normal sleep quality and duration for their age and maintain a delayed, but stable, phase of entrainment to local time.
3. Patients have little or no reported difficulty in maintaining sleep once sleep has begun.
4. Patients have a relatively severe to absolute inability to advance the sleep phase to earlier hours by enforcing conventional sleep and wake times.
5. Sleep-wake logs and/or actigraphy monitoring for at least two weeks document a consistent habitual pattern of sleep onsets, usually later than 2 a.m., and lengthy sleeps.
6. Occasional noncircadian days may occur (i.e., sleep is "skipped" for an entire day and night plus some portion of the following day), followed by a sleep period lasting 12 to 18 hours.
7. The symptoms do not meet the criteria for any other sleep disorder causing inability to initiate sleep or excessive sleepiness.
8. If any of the following laboratory methods is used, it must demonstrate a delay in the timing of the habitual sleep period: 1) Twenty-four-hour polysomnographic monitoring (or by means of two consecutive nights of polysomnography and an intervening multiple sleep latency test), 2) Continuous temperature monitoring showing that the time of the absolute temperature nadir is delayed into the second half of the habitual (delayed) sleep episode.

Some people with the abnormality adapt their lives to the delayed sleep phase, avoiding common business hours (e.g., 9 a.m. to 5 p.m.) as much as possible. They have the disorder, but for them it is not a disability. The ICSD's severity criteria, all of them "over at least a one-month period", are:

- Mild: Two hour delay associated with little or mild impairment of social or occupational functioning.
- Moderate: Three hour delay associated with moderate impairment.
- Severe: Four hour delay associated with severe impairment.

Some features of DSPS which distinguish it from other sleep disorders are:

- People with DSPS have at least a normal—and often much greater than normal—ability to sleep during the morning, and sometimes in the afternoon as well. In contrast, those with chronic insomnia do not find it much easier to sleep during the morning than at night.
- People with DSPS fall asleep at more or less the same time every night, and sleep comes quite rapidly if the person goes to bed near the time he or she usually falls asleep. Young children with DSPS resist going to bed before they are sleepy, but the bedtime struggles disappear if they are allowed to stay up until the time they usually fall asleep.
- DSPS patients can sleep well and regularly when they can follow their own sleep schedule, e.g. on weekends and during vacations.
- DSPS is a chronic condition. Symptoms must have been present for at least one month before a diagnosis of DSPS can be made.

Attempting to force oneself onto daytime society's schedule with DSPS has been compared to constantly living with 6 hours of jet lag; the disorder has, in fact, been referred to as "social jet lag". Often, sufferers manage only a few hours sleep a night during the working week, then compensate by sleeping until the afternoon on weekends. Sleeping in on weekends, and/or taking long naps during the day, may give people with the disorder relief from daytime sleepiness but may also perpetuate the late sleep phase.

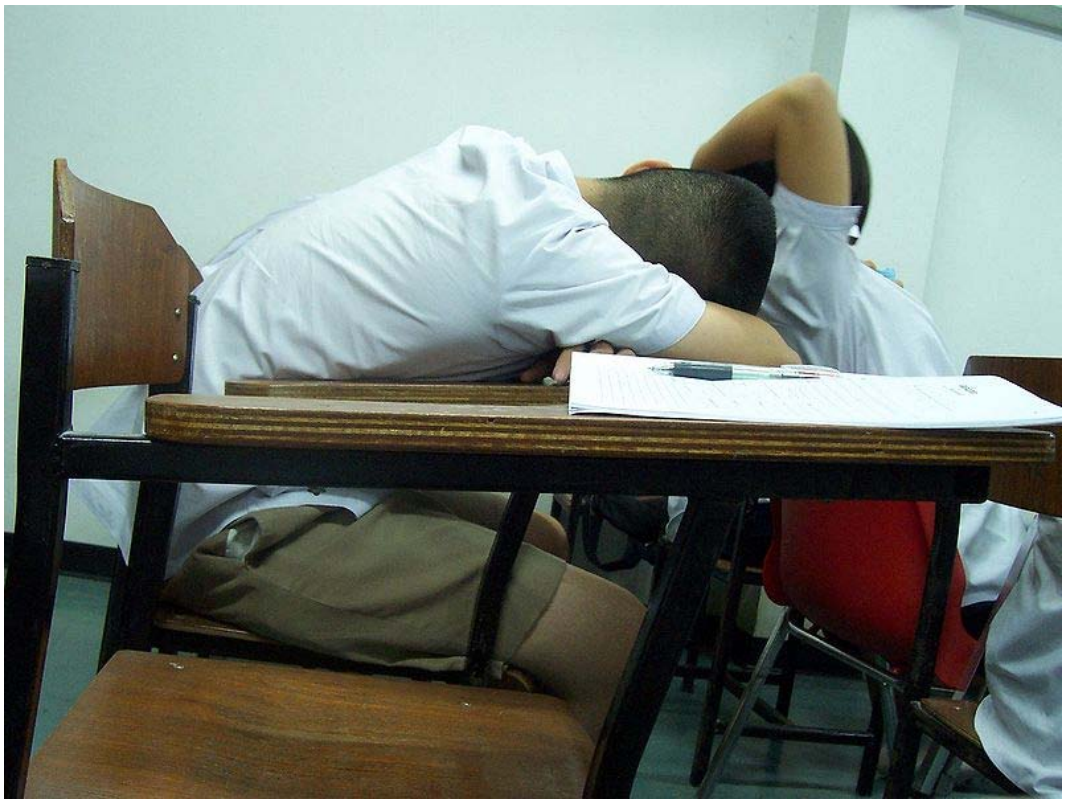
People with DSPS can be called extreme night owls. They feel most alert and say they function best and are most creative in the evening and at night. DSPS patients cannot simply force themselves to sleep early. They may toss and turn for hours in bed, and sometimes not sleep at all, before reporting to work or school. Less extreme and more flexible night owls, and indeed morning larks, are within the normal chronotype spectrum.

By the time DSPS patients seek medical help, they usually have tried many times to change their sleeping schedule. Failed tactics to sleep at earlier times may include maintaining proper sleep hygiene, relaxation techniques, early bedtimes, hypnosis, alcohol, sleeping pills, dull reading, and home remedies. DSPS patients who have tried using sedatives at night often report that the medication makes them feel tired or relaxed, but that it fails to induce sleep. They often have asked family members to help wake them in the morning, or they have used several alarm clocks. As the syndrome occurs in childhood and is most common in adolescence, it is often the patient's parents who initiate seeking help, after great difficulty waking their child in time for school.

The current formal name established in the second edition of the International Classification of Sleep Disorders is **circadian rhythm sleep disorder, delayed sleep phase type**; the preferred common name is delayed sleep-phase disorder.

Prevalence

About 0.15% of adults, three in 2,000, have DSPS. Using the strict ICSD diagnostic criteria, a random study in 1993 of 7700 adults (aged 18–67) in Norway estimated the prevalence of DSPS at 0.17%. A similar study of 1525 adults (aged 15–59) in Japan estimated its prevalence at 0.13%.



Sleepy students

DSPS is not uncommon among teenagers; at least one study has indicated that the prevalence of DSPS among adolescents is as high as 7%. Among adolescents, boys predominate, while the gender distribution shows equal numbers of women and men in adults.

A marked delay of sleep patterns is a normal feature of the development of adolescent humans. According to Mary Carskadon, both circadian phase and homeostasis (the accumulation of sleep pressure during the wake period) contribute to a DSPS-like condition in post-pubertal as compared to pre-pubertal adolescents.

Physiology

DSPS is a disorder of the body's timing system—the biological clock. Individuals with DSPS might have an unusually long circadian cycle, might have a reduced response to the re-setting effect of daylight on the body clock and/or may respond overly to the delaying effects of evening light and too little to the advancing effect of light earlier in the day. In support of the increased sensitivity to evening light hypothesis, "the percentage of melatonin suppression by a bright light stimulus of 1,000 lux administered 2 hours prior to the melatonin peak has been reported to be greater in 15 DSPS patients than in 15 controls."

People with normal circadian systems can generally fall asleep quickly at night if they slept too little the night before. Falling asleep earlier will in turn automatically help to advance their circadian clocks due to decreased light exposure in the evening. In contrast, people with DSPS are unable to fall asleep before their usual sleep time, even if they are sleep-deprived. Sleep deprivation does not reset the circadian clock of DSPS patients, as it does with normal people.

People with the disorder who try to live on a normal schedule cannot fall asleep at a "reasonable" hour and have extreme difficulty waking because their biological clocks are not in phase with that schedule. Normal people who do not adjust well to working a night shift have similar symptoms (diagnosed as shift-work sleep disorder, SWSD).

In most cases, it is not known what causes the abnormality in the biological clocks of DSPS patients. DSPS tends to run in families, and a growing body of evidence suggests that the problem is associated with the hPer3 (human period 3) gene. There have been several documented cases of DSPS and non-24-hour sleep-wake syndrome developing after traumatic head injury.

There have been a few cases of DSPS developing into non-24-hour sleep-wake syndrome, a more severe and debilitating disorder in which the individual sleeps later each day. It has been suggested that, instead of (or perhaps in addition to) a reduced reaction to light in the morning, an abnormal *over-sensitivity* to light in the late evening might contribute to the odd non-circadian pattern.

Diagnosis

p.m.	Wed	Thu	Fri	Sat	Sun	Mon	Tue
a.m.	**Thu**	**Fri**	**Sat**	**Sun**	**Mon**	**Tue**	**Wed**

A **sleep diary** with nighttime in the middle and the weekend in the middle, the better to notice trends

DSPS is diagnosed by a clinical interview, actigraphic monitoring and/or a sleep diary kept by the patient for at least three weeks. When polysomnography is also used, it is primarily for the purpose of ruling out other disorders such as narcolepsy or sleep apnea. If a person can, on her/his own with just the help of alarm clocks and will-power, adjust to a daytime schedule, the diagnosis is not given.

DSPS is frequently misdiagnosed or dismissed. It has been named as one of the sleep disorders most commonly misdiagnosed as a primary psychiatric disorder. DSPS is often confused with: psychophysiological insomnia; depression; psychiatric disorders such as schizophrenia, ADHD or ADD; other sleep disorders; or school refusal. Practitioners of sleep medicine point out the dismally low rate of accurate diagnosis of the disorder, and have often asked for better physician education on sleep disorders.

Management

Treatment, a set of management techniques, is specific to DSPS. It is different from treatment of insomnia, and recognizes the patients' ability to sleep well on their own schedules, while addressing the timing problem. Success, if any, may be partial; for example, a patient who normally awakens at noon may only attain a wake time of 10 or 10:30 with treatment and follow-up. Being consistent with the treatment is paramount.

Before starting DSPS treatment, patients are often asked to spend at least a week sleeping regularly, without napping, at the times when the patient is most comfortable. It is important for patients to start treatment well-rested.

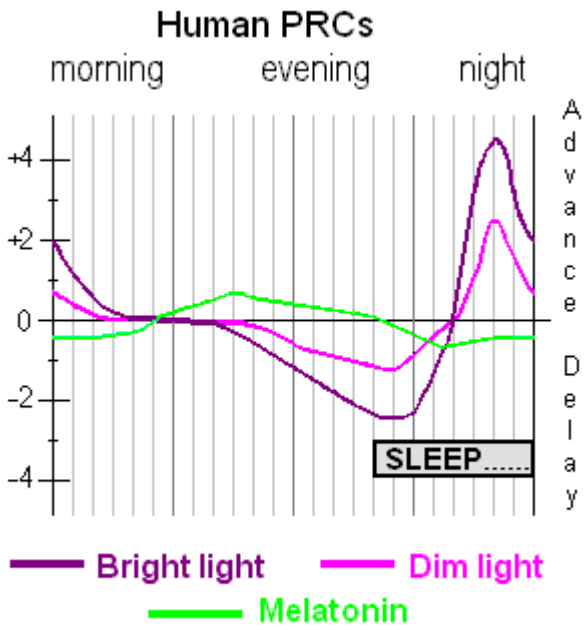
Treatments that have been reported in the medical literature include:

Light therapy (phototherapy) with a full spectrum lamp or portable visor, usually 10,000 lux for 30–90 minutes at the patient's usual time of spontaneous awakening, or shortly before (but not long before), which is in accordance with the phase response curve (PRC) for light. The use of an LED light therapy device can reduce this to 15–30 minutes. Sunlight can also be used. Only experimentation, preferably with specialist help, will show how great an advance is possible and comfortable. For maintenance, some patients must continue the treatment indefinitely, some may reduce the daily treatment to 15 minutes, others may use the lamp, for example, just a few days a week or just every third week. Whether the treatment is successful is highly individual. Light therapy generally requires adding some extra time to the patient's morning routine. Patients with a family history of macular degeneration are advised to consult with an eye doctor. The use of exogenous melatonin administration in conjunction with light therapy is common.

Dim lights in the evening, sometimes called darkness therapy. Just as bright light upon awakening should advance one's sleep-phase, bright light in the evening and night delays it. One might be advised to keep lights dim the last hours before bedtime and even wear sunglasses or amber-colored goggles. Attaining an earlier sleep onset, in a dark room with eyes closed, effectively blocks a period of phase-delaying light. An understanding of this is a motivating factor in treatment.

Chronotherapy, which is intended to reset the circadian clock by manipulating bedtimes. Often, chronotherapy must be repeated every few months to maintain results, and its safety is uncertain. It can be one of two types. The most common consists of going to bed two or more hours *later* each day for several days until the desired bedtime is reached. A modified chronotherapy (Thorpy, 1988) is called controlled sleep deprivation with phase advance, SDPA. One stays awake one whole night and day, then goes to bed 90 minutes *earlier* than usual and maintains the new bedtime for a week. This process is repeated weekly until the desired bedtime is reached.

Melatonin taken an hour or so before usual bedtime may induce sleepiness.



Phase response curves for light and for melatonin administration

Taken this late, it does not, of itself, affect circadian rhythms, but a decrease in exposure to light in the evening is helpful in establishing an earlier pattern. In accordance with its phase response curve (PRC), a very small dose of melatonin can also, or instead, be taken some hours earlier as an aid to resetting the body clock; it must then be so small as to not induce excessive sleepiness.

Side effects of melatonin may include disturbance of sleep, nightmares, daytime sleepiness and depression, though the current tendency to use lower doses has decreased such complaints. Large doses of melatonin can even be counterproductive: Lewy et al. provide support to the "idea that too much melatonin may spill over onto the wrong zone of the melatonin phase-response curve." The long-term effects of melatonin administration have not been examined. In some countries the hormone is available only by prescription or not at all. In the United States and Canada, melatonin is freely available as a dietary supplement. The prescription drug Rozerem (ramelteon) is a melatonin analogue that selectively binds to the melatonin MT_1 and MT_2 receptors and, hence, has the possibility of being effective in the treatment of DSPS.

A review by a US government agency found little difference between melatonin and placebo for most primary and secondary sleep disorders. The one exception, where melatonin is effective, is the "circadian abnormality" DSPS.

Modafinil (Provigil) is approved in the US for treatment of shift-work sleep disorder, which shares some characteristics with DSPS, and a number of clinicians are prescribing it for DSPS patients. Modafinil does not deal with underlying causes of DSPS, but it may improve a sleep-deprived patient's quality of life. Taking modafinil less than 12 hours

before the desired sleep onset time will likely exacerbate the symptoms by delaying the sleep/wake cycle.

Trazodone successfully treated DSPS in one elderly man.

Vitamin B_{12} was, in the 1990s, suggested as a remedy for DSPS/DSPD, and can still be found to be recommended by many sources. Several case reports were published. However, a review for the American Academy of Sleep Medicine in 2007 concluded that no benefit was seen from this treatment.

A strict schedule and good sleep hygiene are essential in maintaining any good effects of treatment. With treatment, some people with mild DSPS may sleep and function well with an early sleep schedule. Caffeine and other stimulant drugs to keep a person awake during the day may not be necessary, and should be avoided in the afternoon and evening, in accordance with good sleep hygiene. A chief difficulty of treating DSPS is in *maintaining* an earlier schedule after it has been established. Inevitable events of normal life, such as staying up late for a celebration or having to stay in bed with an illness, tend to reset the sleeping schedule to its intrinsic late times.

Prognosis

Adaptation to late sleeping times

Long-term success rates of treatment have seldom been evaluated. However, experienced clinicians acknowledge that DSPS is extremely difficult to treat. One study of 61 DSPS patients with mean sleep onset at about 3 a.m. and mean waking time of about 11:30 a.m., followed up with questionnaires to the subjects a year later. Good effect was seen *during* the 6-week treatment with a daily, very large dose (5 mg), of melatonin. Follow-up showed that over 90% had relapsed to pretreatment sleeping patterns within the year, 28.8% reporting that the relapse occurred within one week. The milder cases retained changes significantly longer than the more severe cases.

Working the evening or night shift, or working at home, makes DSPS less of an obstacle for some. Many of these people do not describe their pattern as a "disorder". Some DSPS individuals nap, even taking 4–5 hours of sleep in the morning and 4–5 in the evening. DSPS-friendly careers can include security work, work in theater, the entertainment industry, hospitality work in restaurants, hotels or bars, call center work, nursing, taxi or truck driving, the media, and freelance writing, translation, IT work, or medical transcription.

Some people with the disorder are unable to adapt to earlier sleeping times, even after many years of treatment. Sleep researchers have proposed that the existence of untreatable cases of DSPS be formally recognized as a "sleep-wake schedule disorder disability", an invisible disability.

Rehabilitation for DSPS patients includes acceptance of the condition, and choosing a career that allows late sleeping times, or running their own home business because it allows flexible hours. In a few schools and universities, students with DSPS have been able to arrange to take exams at times of day when their concentration levels may be good.

> “ Patients suffering from SWSD disability should be encouraged to accept the fact that they suffer from a permanent disability, and that their quality of life can only be improved if they are willing to undergo rehabilitation. It is imperative that physicians recognize the medical condition of SWSD disability in their patients and bring it to the notice of the public institutions responsible for vocational and social rehabilitation. ”

In the United States, the Americans with Disabilities Act requires that employers accommodate employees with sleeping disorders by providing appropriate accommodations. In the case of DSPS, this requires that the employer accommodate later working hours for jobs normally performed on a "9-to-5" work schedule.

Impact on patients

Lack of public awareness of the disorder contributes to the difficulties experienced by people with DSPS, who are commonly stereotyped as undisciplined or lazy. Parents may be chastised for not giving their children acceptable sleep patterns, and schools and workplaces rarely tolerate chronically late, absent, or sleepy students and workers, failing to see them as having a chronic illness.

> “ By the time DSPS sufferers receive an accurate diagnosis, they often have been misdiagnosed or labelled as lazy and incompetent workers or students for years. Misdiagnosis of circadian rhythm sleep disorders as psychiatric conditions causes considerable distress to patients and their families, and leads to some patients being inappropriately prescribed psychoactive drugs. For many patients, diagnosis of DSPS is itself a life-changing breakthrough. ”

As DSPS is so little-known and so misunderstood, support groups may be important for information and self-acceptance.

People with DSPS who force themselves to live on a normal 9-5 day "are not often successful and may develop physical and psychological complaints during waking hours, i.e. sleepiness, fatigue, headache, decreased appetite, or depressed mood. Patients with [Circadian Rhythm Sleep Disorders] often have difficulty maintaining ordinary social lives, and some of them lose their jobs or fail to attend school.

Comorbidity

In the DSPS cases reported in the literature, about half of the patients have suffered from clinical depression or other psychological problems, about the same proportion as among patients with chronic insomnia. According to the ICSD:

> “Although some degree of psychopathology is present in about half of adult patients with DSPS, there appears to be no particular psychiatric diagnostic category into which these patients fall. Psychopathology is not particularly more common in DSPS patients compared to patients with other forms of "insomnia." ... Whether DSPS results directly in clinical depression, or vice versa, is unknown, but many patients express considerable despair and hopelessness over sleeping normally again.”

A direct neurochemical relationship between sleep mechanisms and depression is another possibility.

It is conceivable that DSPS often has a major role in causing depression because it can be such a stressful and misunderstood disorder. A recent study from the University of California, San Diego found no association of bipolar disorder (history of mania) with DSPD, and it states that there may be

> “behaviorally-mediated mechanisms for comorbidity between DSPD and depression. For example, the lateness of DSPD cases and their unusual hours may lead to social opprobrium and rejection, which might be depressing...”

The fact that half of DSPS patients are not depressed indicates that DSPS is not merely a symptom of depression. Sleep researcher M. Terman has suggested that those who follow their internal circadian clocks may be less likely to suffer from depression than those try to live on a different schedule.

DSPS patients who also suffer from depression may be best served by seeking treatment for both problems. There is some evidence that effectively treating DSPS can improve the patient's mood and make antidepressants more effective.

Vitamin D deficiency has been linked to depression. As it is a condition which comes from lack of exposure to sunlight, anyone who does not get enough sunlight exposure during the daylight hours could be at risk.

Accommodations

United States

According to the Americans with Disabilities Act of 1990, "disability" is defined as a "physical or mental impairment that substantially limits one or more major life activities". "Sleeping" is defined as a "major life activity" in § 12102(2)(a) of the statute.