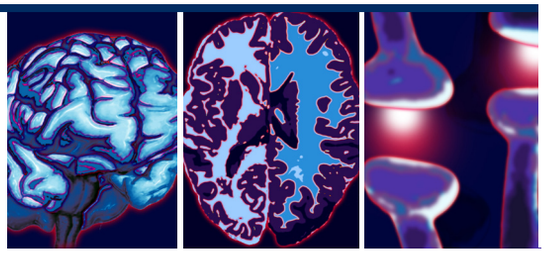
REVIEW



Focus issues in dysthymia

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Practice points

- Dysthymia (dysthymic disorder) is characterized by chronic low grade depression lasting for at least 2 years in adults and 1 year in children and adolescents.
- The causation of dysthymia is multifactorial and underlying personality plays a role.
- In adults with dysthymia, substance abuse, major depressive disorder, anxiety disorders (particularly panic disorder) and borderline personality disorder may present as comorbid illnesses.
- Common comorbidities with dysthymia in children and adolescents are attention deficit hyperkinetic disorder, conduct disorder, anxiety disorders, learning disorders and mental retardation.
- Dysthymia coexists along with major depressive disorder as double depression.
- Treatment of dysthymia is similar to that of major depressive disorder.
- Selective serotonin reuptake inhibitors are commonly recommended (both for children and adults) for treatment of dysthymia.
- Cognitive behaviour therapy and interpersonal therapy are effective in the treatment of dysthymia.
- Combination therapy (pharmacotherapy and psychotherapy) is more effective than either pharmacotherapy or psychotherapy in isolation in treatment of dysthymia.

SUMMARY Dysthymia (dysthymic disorder) is one of the most commonly encountered psychiatric illnesses in day-to-day practice, affecting approximately one in every 20 people worldwide. Intensity of depressive content and impairment is less in dysthymia in comparison to major depressive disorder, but the management of dysthymia is similar to that of depression. Underlying personality plays a major role in dysthymia. This article focusses on current issues including management and research works of dysthymia. The issue of placement of dysthymia in current classificatory systems is also addressed.

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Dysthymia (dysthymic disorder) is described as a depressive mood disorder that follows a chronic course. Dysthymia and major depressive disorder are two different entities. Dysthymia is not a sequel of well-defined major depressive episodes [1].

What is coined as dysthymia in International Classification of Diseases (ICD)-10 [101] is known as dysthymic disorder in the *Diagnostic and Statistical Manual of Mental Disorders* (DSM)-IV-TR. Onset of dysthymia is insidious and in most cases early (onset before the age of 21 years) [1]. Late-onset (onset at or after the age of 21 years) dysthymia is relatively rare. Early-onset dysthymia is associated with a higher risk of melancholia, more impairment, higher risk of recurrence of major depressive episodes and a higher risk of substance abuse in comparison to late-onset dysthymia [2].

Risk factors of early-onset dysthymia include early trauma, family history, attention deficit hyperactivity disorder and incomplete recovery from major depression [2]. Risk factors of late-onset dysthymia include significant life stressors (e.g., death of a loved one/accident) and substance abuse [2].

Dysthymia is more common in females than males. Studies revealed that there is impairment in quality of life, functioning, social support and marital adjustment among patients with dysthymia [3–9]. Impairments in dysthymia are comparatively less in comparison to major depressive disorder. Dysthymia was previously known as neurotic depression, chronic minor depression and characterological depression [1].

Niculescu and Akisal described dysthymia by dividing it into two subcategories [10]. The first subcategory anergic dysthymia is characterized by a feeling of anergia (lack of energy), anhedonia, loss of libido, weight loss and excessive sleep. This variant of dysthymia is common in males. Patients respond better to dopaminergic and noradrenergic agents. The second subcategory, anxious dysthymia, is characterized by a feeling of subjective restlessness, sense of insecurity, impulsivity and low self-esteem. This variant is common in females and responds well to serotonergic agents (selective serotonin reuptake inhibitors [SSRIs]) [10].

It is not a single factor, but rather many etiological factors that are responsible for the development of dysthymia. The etiology of dysthymia is quite similar to that of major depressive disorder. Important etiological factors are outlined in **Box 1** [11].

Box 1. Etiological factors of dysthymia.

- Biological factors:
  - Genetic linkage, twin studies, neurochemical mechanisms
- Sleep studies:
  - Increased rapid eye movement density and decreased rapid eye movement latency
- Neuroendocrinologic factors:
  - Involvement of the thyroid and adrenal axes
- Psychosocial factors:
  - Difficulty in adaptation to adolescence and early adulthood
  - Conflict in oral and anal sadistic phase
  - Interpersonal disappointment in early life leading to defective ego development
- Cognitive theory
  - Mismatch between reality and fantasy leading to decreased self-esteem

Data taken from [11].

Epidemiology

Approximately one in every 20 people encounters dysthymia in their life time with lifetime prevalence rate of 3–6% (average 5%) [12]. The lifetime prevalence of major depressive disorder is more (5–17%; average: 12%) than that of dysthymia [12]. Among all psychiatric illnesses, depression is the most commonly encountered with an overall prevalence of 9–20% [13]. Approximately 1.5% of US citizens aged 18 years or above experience dysthymia in a year [14]. The National Health and Nutrition Examination Survey (NHANES) III, found that dysthymia is more prevalent among African–Americans and Mexican–Americans than among Caucasians [15].

According to data collected by the National Institute of Mental Health (1988) for the Epidemiological Catchment Area Study, in the general population, dysthymia has the lifetime prevalence of 3.1% [16]. Kessler and colleagues, in their survey (National Comorbidity Survey) reported the lifetime prevalence to be 4.8% among men and 8% among women (average 6.4%) [17]. Women are at higher risk of developing dysthymia than men (female:male ratio is approximately 3:1). Dysthymia is common among individuals with a positive family history of major depression in first-degree relatives [1]. Few studies are available regarding racial differences in symptomatology of dysthymia. Minimal research has been performed to define differences in frequency and symptoms between races.

Patients of dysthymia are likely to develop a major depressive episode during the course of illness. Approximately 80% of the patients will

be diagnosed with major depression in their lifetime [18], while 25–50% of the patients with major depression have comorbid dysthymia [19]. When a major depressive episode overlaps with dysthymia, the condition is called double depression [20]. In double depression there is always a risk of prolongation of the major depressive episode and complete recovery is unlikely [21]. Laptook *et al.* had conducted a 10-year follow-up study on patients of dysthymia who experienced major depression [22]. They found that the majority (70%) of the patients had short recovery period and the major depressive episode followed a chronic course. The relapse rate following recovery was also as high as 70% [22].

Diagnosis & management

Currently, the DSM-IV-TR [1] mentions that a diagnosis of dysthymia includes depressed mood, accompanied with two or more of the following: poor appetite or overeating, insomnia or hypersomnia, low energy or fatigue, low self-esteem, poor concentration or difficulty making decisions, and feelings of hopelessness. The mood can be irritable in children and adolescents. These symptoms persist most of the day and last over a period of 2 years or more. In children and adolescents, duration of at least 1 year is sufficient to make the diagnosis of dysthymia. Individuals may have symptom-free periods but not for more than two consecutive months. The symptoms are generally milder but longer lasting than those of a major depressive episode. If the symptoms are associated with another psychiatric impairment such as schizophrenia, manic episodes or organic psychosis, a diagnosis of dysthymia does not apply. Individuals with this disorder must not have had a major depressive episode during the first 2 years of the disturbance unless a full remission occurred without significant signs or symptoms for 2 months before development of the dysthymia. Patients are diagnosed with chronic major depression if their depressive symptoms are caused by major depression and not dysthymia during the first 2 years of the disturbance. If it recurs in a patient with dysthymia after the first 2 years, the patient is diagnosed with double depression. Diagnosis of dysthymia is not made if there is any episode of hypomania, mania, mixed episode, cyclothymia or if the symptoms of dysthymia are secondary to physical illness (hypothyroidism), medication, substance abuse or psychotic disorder. It must cause clinically significant distress or impairment in social, occupational, or other important areas of functioning. As per the ICD-10, depressive personality disorder is also included under the category of dysthymia [101]. It was previously also known by the name of 'melancholic personality disorder'. It was removed from DSM-III and DSM-III-R. In DSM-IV-TR, it is placed under the category of 'personality disorder not otherwise specified' [1]. The differential diagnoses for dysthymia are outlined in **Box 2** [11].

Box 2. Differential diagnoses of dysthymia.

- Minor depressive disorder: contrary to dysthymia it follows an episodic course
- Recurrent brief depressive disorder: differs from dysthymia by its episodic nature and severity
- Double depression: dysthymia with superimposed major depressive disorder
- Substance abuse disorders: substance abuse is significant and the dysthymic state is explainable by substance abuse. A definite temporal correlation between substance abuse and mood symptoms is always present

Data taken from [**11**].

In depressive personality disorder, there is distorted self-image, chronic feeling of low, constant unhappiness, pessimism, humorlessness, self-blame and a proneness for excessive worrying. Most of the features of depressive personality disorder overlap with that of dysthymia, so it is considered a differential diagnosis of dysthymia. Early-onset dysthymia closely resembles depressive personality disorder. The diagnosis of dysthymia is based primarily on somatic symptoms whereas the diagnosis of depressive personality disorder mainly focuses on cognitive and intra-psychic symptoms [102]. Patients of dysthymia may have comorbid depressive personality disorder [23,24]. Functional health status is an important parameter that distinguishes dysthymia from that of depressive personality disorder. Huprich *et al.* in their study in a primary care population found that depressive personality disorder is less associated with functional health status as compared to dysthymia [25]. In adults with dysthymia, substance abuse, major depressive disorder, anxiety disorders (particularly panic disorder) and borderline personality disorder may present as comorbid illnesses [11]. Common comorbidities with dysthymia in children and adolescents are attention deficit hyperkinetic disorder, conduct disorder, anxiety disorders, learning disorders and mental

retardation. In most cases, dysthymia partly responds to treatment although some residual symptoms remain, which are potential risk factors for relapse [26–28]. Another important risk factor for relapse is comorbid personality disorder [29,30]. Avoidant and obsessive–compulsive disorders frequently coexist with dysthymia [31]. Many medical conditions like diabetes mellitus, hypertension and other chronic medical conditions may coexist with dysthymia.

In dysthymia the treatment aims at:

- Improving depressive symptoms
- Reducing risk of development of other mood disorders (e.g., major depressive disorder)
- Improving global psychosocial functioning and overall quality of life

Treatment of dysthymia is almost the same as that of depression. It includes pharmacotherapeutic intervention (antidepressants) and psychotherapy. These treatment modalities can be used alone or in combination.

Pharmacotherapeutic intervention is carried out with antidepressant medications such as tricyclic antidepressants, SSRIs and serotonin (5-HT)–norepinephrine (NE) reuptake inhibitors. Among the antidepressants, serotonergic agents (SSRIs) are found to be highly effective in the treatment of dysthymia [11,32]. SSRIs are the first-line drugs recommended for treatment of dysthymia in children and adolescents [32]. SSRIs are well tolerated by children and adolescents. Therapeutic effects of the SSRIs start in 3–4 weeks. Treatment usually starts at lower doses and continues up to a minimum of 3 months. Gradually the doses are built up, if the patient responds to the treatment then treatment should continue for 2–3 years. Approximately 56% of individuals with dysthymia benefit from antidepressant medication [33]. Commonly prescribed SSRIs for dysthymia are fluoxetine, sertraline and paroxetine (under consideration). One serotonin–norepinephrine reuptake inhibitor found to be effective in dysthymia is venlafaxine [11,34,35]. Although not commonly used to treat the US population, tricyclic antidepressants are found to be effective in dysthymia. Among the tricyclic antidepressants, are commonly tried medications including imipramine and desipramine [36–39].

Antidepressants exert their action mainly through 5-HT or NE receptor modulation. Studies were conducted to find the role of dopamine in the depressive symptom profile of dysthymia. Unfortunately the studies are few in number. The selective D2 and D3 receptor antagonist amisulpride, which has dopamine receptor agonistic properties at low doses, was found to be effective in dysthymia [40–42]. In placebo-controlled trials in patients with dysthymia with or without major depression or those with major depression in partial remission, amisulpride 50 mg/day was more effective than placebo and had similar efficacy to imipramine 100 mg/day or amineptine 200 mg/day according to standard depression rating scales. In trials predominantly in patients with pure dysthymia, amisulpride 50 mg/day was as effective as amitriptyline 25–75 mg/day or fluoxetine 20 mg/day, according to standard depression ratings [43–45].

Among the psychotherapy modalities, cognitive behavior therapy, psychoanalytic psychotherapy, group therapy, family therapy and interpersonal therapy are the most effective modalities of treatment [11]. Cognitive intervention is effective in bringing change in hopelessness, unrealistic expectations and distorted self-image. Supportive psychotherapy improves hopelessness and builds confidence. In children and adolescents, the aforementioned modalities of psychotherapy are found to be effective. During management of dysthymia in a pediatric population, psychoeducation of the family members and psychosocial factors are also important issues that need to be addressed [46]. Recent research on treatment outcomes of patients with dysthymia suggest that treatment with psychotherapy in isolation has the poorest outcome when compared to pharmacotherapy alone and the combined treatment of psychotherapy and pharmacotherapy has the best outcome [47]. A minimum of 18 psychotherapy sessions, at weekly intervals, is found to be effective. Among the different psychotherapy modalities available, cognitive behavior therapy shows better efficacy [48]. Teaching coping skills and relaxation methods to individuals with dysthymia is beneficial.

The Cornell Dysthymia Rating Scale (CDRS) and Hamilton Depression Rating Scale (HDRS) are the most common standard rating scales used to assess the clinical severity of dysthymia [49]. The former scale is a clinician rated scale where as the latter is an observer rated scale. The Global Assessment Scale (GAS) is used to rate the global functioning and Quality of Life scales are used to assess the quality of life [50].

Current controversies

Controversies are ongoing regarding the position of dysthymia in the clinical classificatory system of psychiatry. Initially dysthymia was thought to be a state of chronic mild depression or personality disorder, whereas the current belief concerning dysthymia is that it is a chronic or fluctuating, low-grade (subsyndromal) primary mood disorder [51]. Patients with dysthymia often have experiences of unexplained unhappiness in their early childhood. Whether DSM-IV-TR adequately addresses dysthymia in children and adolescents is a matter of some controversy [52].

In order to find a solution regarding the controversy of dysthymia, attempts have been taken in the upcoming DSM-5, where dysthymia is renamed as chronic depressive disorder [103]. The main reason behind putting dysthymia under the category of chronic depressive disorder is that studies conducted to find out differences between chronic unipolar depression and dysthymia revealed similar history, course and outcome [53–56]. The new domain chronic depressive disorder in DSM-5 highlights the risks of other psychiatric disorders along with its course and risk of recurrence. Placing dysthymia as a chronic depressive disorder will be more advantageous. By doing so much attention will be paid to underlying maladaptive patterns of thinking and behaviors that are sometimes focus of empirically supported cognitive behavioral treatment. It will open the door of research on different components involved in chronic depressive disorder [104]. The work group for DSM-5 proposed diagnostic criteria for chronic depressive disorder, which no longer includes history of major depressive episode in the first 2 years as an exclusion criteria, for making the diagnosis of chronic depressive disorder [103].

Future perspective

Dysthymia was associated with elevated levels of circulating natural killer (NK) cells. Since levels of plasma cortisol, adrenocorticotropin hormone or norepinephrine were not increased in the dysthymic subjects, it is likely that the elevated NK cell number was unrelated to these neuroendocrine measures. In control subjects, circulating NK cells were inversely related to the severity of stressors recently encountered, while in dysthymic patients, stress and coping factors were unrelated to NK cell numbers [57]. Although the preliminary immunological research findings in patients of dysthymia are similar to that of other psychiatric disorders, it has opened the door for research in this area to find out a specific immunologic role in development of dysthymia.

In a study on an elderly population suffering from dysthymia with comorbid major depression conducted in 2004, Devanand *et al.* found that patients with late-onset dysthymia are more at risk of cardiovascular disease compared with patients with early-onset dysthymia who are more prone to develop anxiety disorders [58]. Barbui *et al.* conducted a study on an Italian population in 2006. In this study population of patients with dysthymia, more than 80% of patients had their onset of illness before the age of 21 years (i.e., the early-onset type). It was also found that those individuals with the early-onset type of dysthymia needed more inpatient psychiatric admissions [59]. Keeping in mind the raising trend of stressful lifestyle, substance abuse and increased incidence of depression, it can be predicted that dysthymia will be one of the leading psychiatric illnesses in the coming decades.

Conclusion

Dysthymia is a common mood disorder that often escapes undetected. Few individuals seek treatment for their symptoms. Previously it was often ignored, but currently much importance is given to it due to many reasons (e.g., comorbidities, heritability and premorbid maladjustment with life). Underlying personality plays a key role in development of dysthymia [60–62]. Early life adversity giving rise to a maladaptive personality is a risk factor that is preventable. Current researches on dysthymia aim at finding out its neurochemical and neurobiological basis. Research is also going on different subtypes (i.e., early onset vs late onset, anergic vs anxious) of dysthymia along with potential drug treatment. Current focus is regarding proper placement of dysthymia in the classificatory system of DSM-5 and ICD-11.

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Bibliography

Papers of special note have been highlighted as:

- ■ of interest

1 *Diagnostic and Statistical Manual of Mental Disorders (4th Edition). Text Revision*. American Psychiatric Association, Washington, DC, USA (2000).

2 Sansone RA, Sansone LA: Early- versus late-onset dysthymia. A meaningful clinical distinction? *Psychiatry (Edgmont)* 6(11), 14–17 (2009).

3 Frances AJ: An introduction to dysthymia. *Psychiatr. Ann.* 23, 607–608 (1993).

4 Gupta S, Kulhara P, Verma SK: Quality of life in schizophrenia and dysthymia. *Acta Psychiatr. Scand.* 97(4), 290–296 (1998).

5 Kulhara P, Chopra R: Social support, social dysfunction and stressful life events in neurotic patients. *Indian J. Psychiatry* 38, 23–29 (1996).

6 McCullough JP, McCune KJ, Kaye AL *et al.*: One-year prospective replication study of an untreated sample of community dysthymia subjects. *J. Nerv. Ment. Dis.* 182, 396–401 (1994).

7 Zlotnick C, Kohn R, Keitner G, Della-Grotta SA: The relationship between quality of interpersonal relationships and major depressive disorder: findings from the National Comorbidity Survey. *J. Affect. Disord.* 59(3), 205–215 (2000).

8 Bell B, Chalklin L, Mills M *et al.*: Burden of dysthymia and comorbid illness in adults in a Canadian primary care setting: high rates of psychiatric illness in the offspring. *J. Affect. Disord.* 78(1), 73–80 (2004).

9 Chakrabarti S, Kulhara P, Verma SK: The pattern of burden in families of neurotic patients. *Soc. Psychiatry Psychiatr. Epidemiol.* 28, 172–177 (1993).

10 Niculescu AB 3rd, Akiskal HS: Proposed endophenotypes of dysthymia: evolutionary, clinical and pharmacogenomic considerations. *Mol. Psychiatry* 6(4), 363–366 (2001).

11 Sadock BJ, Alcott V: *Kaplan and Sadock's Synopsis of Psychiatry: Behavioral Sciences/ Clinical Psychiatry (10th Edition).* Lippincott Williams and Wilkins, MD, USA, 562–567 (2007).

12 Sadock BJ, Sadock VA: *Kaplan and Sadock's Comprehensive Text Book of Psychiatry (9th Edition)* Lippincott Williams & Wilkins, MD, USA, 1647 (2009).

13 McDaniel JS, Musselman DL, Proter ML: Depression in patients with cancer. *Arch. Gen. Psychiatry* 52, 89–99 (1995).

14 Kessler RC, Chiu WT, Demler O, Walters EE: Prevalence, severity, and comorbidity of twelve-month DSM-IV disorders in the National Comorbidity Survey Replication (NCS-R). *Arch. Gen. Psychiatry* 62(6), 617–627 (2005).

15 Riolo SA, Nguyen TA, Greden JF, King CA: Prevalence of depression by race/ ethnicity: findings from the National Health and Nutrition Examination Survey III. *Am. J. Public Health* 95(6), 998–1000 (2005).

16 Weissman MM, Leaf PJ, Bruce ML, Florio L: The epidemiology of dysthymia in five communities: rates, risks, comorbidity, and treatment. *Am. J. Psychiatry* 145, 815–819 (1988).

17 Kessler RC, McGonagle KA, Zhao S, Nelson CB, Hughes M: Lifetime and 12-month prevalence of DSM-III-R psychiatric disorders in the United States. Results from the National Comorbidity Survey. *Arch. Gen. Psychiatry* 51, 8–19 (1994).

18 Thase ME: Long-term treatments of recurrent depressive disorders. *Compr. Psychiatry* 53, 32–44 (1992).

19 Hirschfeld RM: Guidelines for the long-term treatment of depression. *J. Clin. Psychiatry* 55, 61–69 (1994).

20 Keller MB, Harrison W, Fawcett JA *et al.*: Treatment of chronic depression with sertraline or imipramine: preliminary blinded response rates and high rates of undertreatment in the community. *Psychopharmacol. Bull.* 31(2), 205–212 (1995).

21 Klein DN, Schwartz JE, Rose S, Leader JB: Five-year course and outcome of dysthymic disorder: a prospective, naturalistic follow-up study. *Am. J. Psychiatry* 157(6), 931–939 (2000).

22 Laptook RS, Klein DN, Dougherty LR: Ten-year stability of depressive personality disorder in Psychiatry. *Am. J. Psychiatry* 163(5), 872–880 (2006).

23 Laptook RS: Depressed outpatients. *Am. J. Psychiatry* 163(5), 865–871 (2006).

■ **Examines depressive personality disorder and dysthymia.**

24 Ryder AG, Schuller DR, Bagby RM: Depressive personality and dysthymia: evaluating symptom and syndrome overlap. *J. Affect Disord.* 91(2–3), 217–227 (2006).

25 Huprich SK, Porcerelli J, Binienda J, Karana D: Functional health status and its relationship to depressive personality disorder, dysthymia, and major depression: preliminary findings. *Depress. Anxiety.* 22(4), 168–176 (2005).

26 Ballenger JC: Clinical guidelines for establishing remission in patients with depression and anxiety. *J. Clin. Psychiatry* 60, 29–34 (1999).

■ **Examines the course of dysthymic disorder.**

27 Tyrer P, Seivewright H, Johnson T: The Nottingham Study of neurotic disorder: predictors of 12-year outcome of dysthymic, panic and generalized anxiety disorder. *Psychol. Med.* 34, 1385–1394 (2004).

28 Klein DN, Shankman SA, Rose S: Ten-year prospective follow-up study of the naturalistic course of dysthymic disorder and double depression. *Am. J. Psychiatry* 163, 872–880 (2006).

29 Hayden EP, Klein DN: Outcome of dysthymic disorder at 5-year follow-up: the effect of familial psychopathology, early adversity, personality, comorbidity, and chronic stress. *Am. J. Psychiatry* 158, 1864–1870 (2001).

30 Pollack MH, Otto MW, Rosenbaum JF *et al.*: Longitudinal course of panic disorder: findings from the Massachusetts General Hospital Naturalistic Study. *J. Clin. Psychiatry* 51, 12–16 (1990).

31 Zimmerman M, Rothschild L, Chelminski I: The prevalence of DSM-IV personality disorders in psychiatric outpatients. *Am. J. Psychiatry* 162, 1911–1918 (2005).

32 Griffiths J, Ravindran AV, Merali Z, Anisman H: Dysthymia: a review of pharmacological and behavioral factors. *Mol. Psychiatry* 5(3), 242–261 (2000).

33 Lima MS, Moncrieff J: Drugs versus placebo for dysthymia. *Cochrane Database Syst. Rev.* 4, CD001130 (2000).

34 Ravindran AV, Charbonneau Y, Zaharia M, Al-Zaid K, Wiens A, Anisman H: Efficacy and tolerability of venlafaxine in the treatment of primary dysthymia. *J. Psychiat. Neurosci.* 23, 288–292 (1998).

35 Harrison W, Rabkin J, Stewart JW, McGrath PJ, Tricamo E, Quitkin F: Phenelzine for chronic depressions: a study of continuation treatment. *J. Clin. Psychiatry* 47, 346–349 (1986).

36 Friedman RA, Markowitz JC, Parides M, Kocsis JH: Acute response of social functioning in dysthymic patients with desipramine. *J. Affect. Disord.* 34, 85–88 (1995).

37 Keller MB, Gelengerg AJ, Hirschfeld RN *et al.*: The treatment of chronic depression, part 2: a double blind, randomized trial of sertraline and imipramine. *J. Clin. Psychiatry* 59, 598–607 (1998).

38 Kocsis JH, Frances AJ, Voss C, Mann JJ, Mason BJ, Sweeney J: Imipramine treatment for chronic depression. *Arch. Gen. Psychiatry* 45, 253–257 (1988).

39 Kocsis JH, Thase M, Koran L, Halbreich U, Yonkers K: Pharmacotherapy of pure dysthymia: sertraline vs imipramine and placebo. *Eur. Neuropsychopharm.* 4(Suppl. 3), S204 (1994).

40 Wise RA: The anhedonia hypothesis: mark III. *Behav. Brain Sci.* 8, 178–186 (1985).

41 Fibiger HC: Neurobiology of depression: focus on dopamine. In: *Depression and Mania: from Neurobiology to Treatment*. Gessa GL, Fratta W, Pani L, Serra G (Eds). Lippincott-Raven, PA, USA, 42 (1995).

42 Kapur S, Mann JJ: Role of the dopaminergic system in depression. *Biol. Psychiatry* 32, 1–17 (1992).

43 Noble S, Benfield P: Amisulpride: a review of its clinical potential in dysthymia. *CNS Drugs* 12(6), 471–483 (1999).

44 Paes de Sousa M: Amisulpride in dysthymia: results of a naturalistic study in general practice. *Eur. Psychiatry* 11(Suppl. 3), 145s–147s (1996).

45 Ravizza L: Amisulpride in medium-term treatment of dysthymia: a six-month, double-blind safety study versus amitriptyline. *J. Psychopharmacol.* 13(3), 248–254 (1999).

■ **Review of nonpharmacological management of dysthymic disorder.**

46 Nobile M, Cataldo GM, Marino C, Molteni M: Diagnosis and treatment of dysthymia in children and adolescents. *CNS Drugs* 17(13), 927–946 (2003).

47 Cuijpers P, van Straten A, Schuurmans J, van Oppen P, Hollon SD, Andersson G: Psychotherapy for chronic major depression and dysthymia: a meta-analysis. *Clin. Psychol. Rev.* 30(1), 51–62 (2010).

48 Gureje O: Dysthymia in a cross-cultural perspective. *Curr. Opin. Psychiatry* 24(1), 67–71 (2011).

49 Hellerstein DJ, Batchelder ST, Lee A, Borisovskaya M: Rating dysthymia: an assessment of the construct and content validity of the Cornell Dysthymia Rating Scale. *J. Affect. Disord.* 71(1–3), 85–96 (2002).

50 Rihmer Z: Dysthymic disorder: implications for diagnosis and treatment. *Curr. Opin. Psychiatry* 12(1), 69–75 (1999).

51 Sajatovic M, Ramirez LF: *Rating Scales in Mental Health (2nd Edition)*. Lexi-Comp, Inc., OH, USA, 176–179 (2003).

52 Masi G, Millepiedi S, Mucci M, Pascale RR, Perugi G, Akiskal HS: Phenomenology and comorbidity of dysthymic disorder in 100 consecutively referred children and adolescents: beyond DSM-IV. *Can. J. Psychiatry* 48(2), 99–105 (2003).

53 Klein DM, Shankman SA, Lewinsohn PM, Rohde P, Seeley JR: Family study of chronic depression in a community sample of young adults. *Am. J. Psychiatry* 161, 646–653 (2004).

54 McCullough JP, Klein DN, Keller MB *et al.*: Comparison of DSM-III major depression and major depression superimposed on dysthymia (double depression): validity of the distinction. *J. Abnormal Psychol.* 109, 419–427 (2000).

55 McCullough JP, Klein DN, Borian FE *et al.*: Group comparisons of DSM-IV subtypes of chronic depression: validity of the distinctions part II. *J. Abnormal Psychol.* 112, 614–622 (2008).

56 Yang T, Dunner D: Differential sub-typing of depression. *Depress. Anxiety* 13, 11–17 (2001).

■ **Highlights classification of dysthymic disorder, and comparison of early- versus late-onset dysthymic disorder.**

57 Ravindran AV, Griffiths J, Merali Z, Anisman H: Primary dysthymia: a study of several psychosocial, endocrine and immune correlates. *J. Affect. Disord.* 40(1–2), 73–84 (1996).

58 Devanand DP, Adorno E, Cheng J *et al.*: Late onset dysthymic disorder and major depression differ from early onset dysthymic disorder and major depression in elderly outpatients. *J. Affect. Disord.* 78, 259–267 (2004).

59 Barbui C, Motterlini N, Garattini L: Health status, resource consumption, and costs of dysthymia. (A multi-center two-year longitudinal study). *J. Affect. Disord.* 90, 181–186 (2006).

60 Klein DN, Riso LP, Donaldson SK *et al.*: Family study of early-onset dysthymia: mood and personality disorders in relatives of outpatients with dysthymia and episodic major depression and normal controls. *Arch. Gen. Psychiatry* 52, 487–496 (1995).

61 Lizardi H, Klein DN, Ouimette PC, Riso LP, Anderson RL, Donaldson SK: Reports of the childhood home environment in early-onset dysthymia and episodic major depression. *J. Abnorm. Psychol.* 104, 132–139 (1995).

62 Pepper CM, Klein DN, Anderson RL, Riso LP, Ouimette PC, Lizardi H: DSM-III-R axis II comorbidity in dysthymia and major depression. *Am. J. Psychiatry* 152, 239–247 (1995).

■ Websites

101 WHO: International Classification of Diseases (10th Edition) (ICD-10) www.who.int/classifications/icd/en/bluebook.pdf

102 University of Michigan Psychology Department: Dysthymic disorder (2006) www.med.umich.edu/depression/dysthymia

103 American Psychiatric Association: DSM-5 Work Groups (2010) www.dsm5.org

104 MEMO on the inclusion of depressive personality disorder in DSM-V (or DSM-5) http://depressivepersonalitydisorder.com/blog/?p=48