

Human Behavior Course 2004

Mood Disorders One Depressive Disorders

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HUMAN BEHAVIOR COURSE 2004

MOOD DISORDERS ONE - SLIDES

LEARNING OBJECTIVES AND STUDY QUESTIONS FOR DISCUSSION.

1. Know the meaning of the terms and concepts listed in slide one to slide 3 below.
2. What is the difference between clinical depression and the everyday depression we all experience from time to time?
3. Name the different depressive disorders and whether they are very common (point prevalence > 5%), common (1-5%) or uncommon (<1%) in the general population.
4. Know whether each depressive disorder is more common in men, more common in women, or occurs in a similar proportion of men and women.
5. 3. Know the diagnostic criteria for major depressive disorder.
6. What is the difference between a major depressive episode and major depressive disorder?
7. What is the difference between dysthymic disorder and major depressive disorder?
8. What is the difference between bipolar 2 and major depressive disorder?
9. Know the subtypes of depression and the key characteristics or defining features of each.
10. Describe the pathogenesis of depression from a biological or neurophysiological perspective. What neurotransmitters, nervous system pathways, other body systems, and brain areas are involved?
11. Know the psychosocial causes of depression when considered from the psychoanalytic, object relations, cognitive, and behavioral perspectives.
12. What factors commonly predispose people to developing depression?
13. Know the basic psychotherapeutic, pharmacological, and somatic therapies used to treat depression.

Slide 1

Depression - Terms & Concepts

- ★ Depressive episode
- ★ Suicide
- ★ Mood disorder due to GMC
- ★ Substance included mood disorder
- ★ Major depressive disorder
- ★ Dysthymic disorder
- ★ Atypical depression
- ★ Seasonal affective disorder
- ★ Melancholic depression
- ★ Double depression
- ★ Premenstrual dysphoric disorder
- ★ Post-psychotic depressive disorder of schizophrenia
- ★ Post-stroke depression
- ★ Postpartum depression
- ★ Bereavement
- ★ Pseudounipolar depression
- ★ Parkinson's disease
- ★ Huntington's disease
- ★ Catatonia
- ★ Rejection sensitivity
- ★ Monoamine oxidase inhibitors
- ★ Selective serotonin reuptake inhibitors
- ★ Anger turned inward
- ★ Unconscious or symbolic loss
- ★ Internalized object representations
- ★ Psychoanalytic psychotherapy
- ★ Short-term therapies
- ★ Interpersonal psychotherapy
- ★ Cognitive therapy
- ★ Automatic thoughts
- ★ Selective abstraction
- ★ Arbitrary inference



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Depression - Terms & Concepts 2

- ★ Absolutist thinking
- ★ Magnification and minimization
- ★ Personalization
- ★ Catastrophic thinking
- ★ Collaborative empiricism
- ★ Cognitive schemas
- ★ Biogenic amine model
- ★ Monoamine theories
- ★ Non-monoamine theories
- ★ Global neurophysiologic theories
- ★ Neurophysiologic theories
- ★ Stress diathesis model
- ★ Antidepressant response versus remission
- ★ Phenelzine (Nardil)
- ★ Tranylcypromine (Parnate)
- ★ Tyramine reaction
- ★ Serotonin syndrome
- ★ Meperidine (Demerol)
- ★ Selegiline (Deprenyl)
- ★ Moclobemide
- ★ Imipramine
- ★ Amitriptyline
- ★ Doxepin
- ★ Desipramine
- ★ Nortriptyline
- ★ Secondary versus tertiary amines
- ★ Clomipramine
- ★ Antidepressant overdose
- ★ Fluoxetine
- ★ Paroxetine
- ★ Fluvoxamine
- ★ Amoxapine
- ★ Yohimbine



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Depression - Terms & Concepts 3

- ★ Cyproheptadine
- ★ Amantadine
- ★ Cytochrome P450 system
- ★ Bupropion (Wellbutrin)
- ★ Venlafaxine (Effexor)
- ★ Duloxetine (Cymbalta)
- ★ Trazodone (Desyrel)
- ★ Nefazodone (Serzone)
- ★ Mirtazepine (Remeron)
- ★ Buspirone (BuSpar)
- ★ Dextroamphetamine
- ★ Methylphenidate
- ★ Pemoline
- ★ Electroconvulsive therapy (ECT)
- ★ ECT indications
- ★ ECT complication risks
- ★ ECT adverse effects
- ★ Stages of depression treatment
- ★ Acute phase
- ★ Continuation phase
- ★ Maintenance phase
- ★ Response
- ★ Remission
- ★ Relapse
- ★ Recovery
- ★ Recurrence



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Epidemiology of Major Depressive Disorder

- ★ 12-month prevalence rate ~ 7%
- ★ Lifetime prevalence ~ 15%
- ★ Recurrence rate ~ 75%
- ★ 1-year symptom duration ~ 40%
- ★ Mania ~ 5-10%
- ★ Suicide ~ 15% lifetime occurrence



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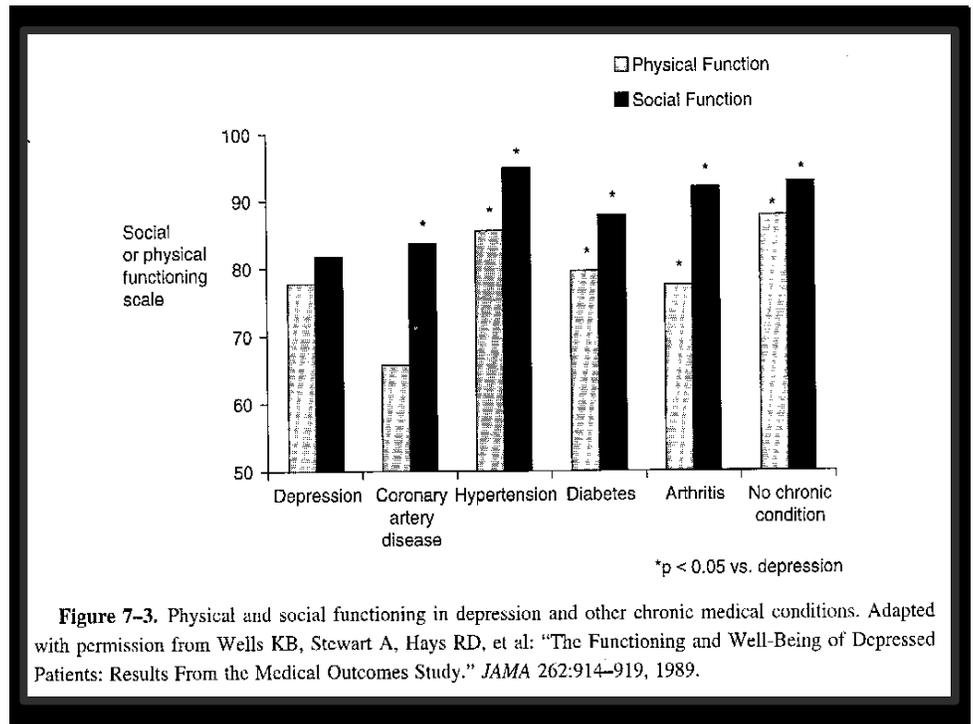
Burden of Depression

- ★ Annual cost (direct & indirect) in U.S. \$43.7 Billion
- ★ Half of depression care occurs in medical settings
- ★ A fifth of depression care occurs in specialty mental health care settings
- ★ MDD sufferers often present to their doctors with vague physical symptoms causing MDD to go undetected or untreated



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Simon, 1999; Regier et al, 1993; Regier et al, 1978



30 Leading Worldwide Causes of Disability WHO Global Burden of Disease Study *

<u>RANK</u>	<u>DISORDER</u>	<u>DALY x 10⁴</u>
1	Lower Respiratory Tract Infections	112.9
2	Diarrheal Diseases	99.6
3	Perinatal Disorders	92.3
4	Unipolar Major Depression	50.8
5	Ischemic Heart Disease	46.7
16	War Injuries	20.0
17	Self-Inflicted Injuries	19.0
19	Violence	17.5
20	Alcohol Use	16.7
22	Bipolar Disorder	14.3
26	Schizophrenia	12.8
28	HIV	11.2
29	Diabetes Mellitus	11.1
30	Asthma	10.8



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* Murry, Lopez. *Lancet* 1997; 349:1436-42

Health Care Costs Among Employees of a Major US Corporation in 1995

TABLE 2. Health Care Costs Incurred by 15,153 Employees of a Major U.S. Corporation Who Filed Health Claims in 1995

Disorder	Cost of Mental Health Care ^a			Cost of Non-Mental-Health Care ^d			Total Health Care Cost ^e		
	Mean (dollars) ^b	Difference From Depression ^c		Mean (dollars) ^b	Difference From Depression ^c		Mean (dollars) ^b	Difference From Depression ^c	
		t	p		t	p		t	p
Depressive disorder (N=412)	1,341			3,032			4,373		
Diabetes (N=203)	29	-22.6	<0.001	4,341	2.98	0.03	4,371	0.00	1.00
Heart disease (N=715)	38	-31.5	<0.001	4,080	3.34	0.01	4,117	-0.80	0.97
Hypertension (N=689)	107	-29.9	<0.001	3,558	1.65	0.56	3,666	-2.18	0.25
Back problems (N=349)	38	-26.8	<0.001	3,337	0.83	0.96	3,376	-2.66	0.08
All others (N=12,785)	24	-39.2	<0.001	925	-8.27	<0.001	949	-13.2	<0.001

^a Proportion of variance explained by the model: R²=9.9% (df=14,360 for each t test).

^b Adjusted for age, sex, race, income, geographic region, education, salary, and tenure with the corporation.

^c Adjusted costs compared with t tests; p values calculated by using the Tukey method of post hoc comparisons.

^d Proportion of variance explained by the model: R²=6.0% (df=14,360 for each t test).

^e Proportion of variance explained by the model: R²=6.5% (df=14,360 for each t test). Calculated as separate model; therefore, may not represent exact sum of mental and non-mental-health costs.



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Druss, Rosenheck, and Sledge, Aug 2000 Am J Psychiatry

Sick Days and Total Employer Costs Among Employees of a Major US Corporation in 1995

TABLE 3. Sick Days and Total Cost Incurred by Employees of a Major U.S. Corporation Who Filed Health Claims and Had Work Data Available in 1995

Disorder	Sick Days (N=9,398) ^a			Total Per Capita Health and Disability Costs (N=9,398) ^d			Total Costs to the Corporation (million dollars) ^e
	Mean ^b	Difference From Depression ^c		Mean (dollars) ^b	Difference From Depression ^c		
		t	p		t	p	
Depressive disorder (N=412)	9.86			5,415			2.2
Diabetes (N=203)	7.17	-2.91	0.04	5,472	0.10	1.00	1.1
Heart disease (N=715)	7.47	-3.27	0.01	5,523	0.24	1.00	3.9
Hypertension (N=689)	5.39	-6.26	<0.001	3,732	-3.88	0.002	2.6
Back problems (N=349)	7.21	-2.90	0.04	4,388	-1.96	0.36	1.5
All others (N=12,785)	3.32	3.31	<0.001	1,292	-11.3	<0.001	16.6

^a Proportion of variance explained by the model: R²=6.0% (df=8,922 for each t test).

^b Adjusted for age, sex, race, income, geographic region, education, salary, and tenure with the corporation.

^c Adjusted costs compared with t tests; p values calculated by using the Tukey method for post hoc comparisons.

^d Proportion of variance explained by the model: R²=8.6% (df=8,922 for each t test).

^e Per capita cost multiplied by number of employees with disorder. Because each total represented only one measurement, tests of statistical significance of differences among total costs across diseases were not performed.



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Druss, Rosenheck, and Sledge, Aug 2000 Am J Psychiatry

Impact of Comorbidity of Depression & Medical Disorders Among Employees of a Major US Corporation in 1995

TABLE 4. Impact of Comorbidity of Depressive Disorder and Four General Medical Disorders Incurred by Employees of a Major U.S. Corporation Who Filed Health Care Claims in 1995

Disorder	Health Care Cost ^a			Sick Days ^d			Total Per Capita Health and Disability Costs ^e		
	Mean (dollars) ^b	Difference From All Others ^c		Mean ^b	Difference From All Others ^c		Mean (dollars) ^b	Difference From All Others ^c	
		t	p		t	p		t	p
Diabetes, heart disease, hypertension, or back problems only (N=1,956)	3,853	22.9	<0.001	6.64	12.50	<0.001	4,646	20.2	<0.001
Depressive disorder only (N=312)	3,417	-8.61	<0.001	8.79	3.19	0.01	4,675	8.4	<0.001
Both (N=100)	7,407	6.73	<0.001	13.48	5.44	<0.001	7,906	8.9	<0.001
All others (12,785)	949			3.32			1,292		

^a Proportion of variance explained by the model: R²=6.7% (df=14,362 for each t test).

^b Adjusted for age, sex, race, income, geographic region, education, salary, and tenure with the corporation.

^c Adjusted costs compared with t tests; p values calculated by using the Tukey method for post hoc comparisons.

^d Proportion of variance explained by the model: R²=6.0% (df=8,924 for each t test).

^e Proportion of variance explained by the model: R²=8.5% (df=8,924 for each t test).



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Druss, Rosenheck, and Sledge, Aug 2000 Am J Psychiatry

Hidden Burden to Primary Medical Care

Number of Symptoms	Number of Patients	Psychiatric Disorder N (%)		
		Anxiety	Mood	Any
<i>Physical (N=1000)</i>				
0-1	215	2 (1)	5 (2)	16 (7)
2-3	225	17 (7)	27 (12)	50 (22)
4-5	191	25 (13)	44 (23)	67 (35)
6-8	230	68 (30)	100 (44)	140 (61)
9+	130	68 (48)	84 (80)	113 (81)
<i>Somatoform (N=900)</i>				
0	654	68 (10)	107 (16)	102 (25)
1-2	143	42 (29)	60 (42)	74 (52)
3-5	87	35 (40)	40 (46)	77 (89)
6+	49	40 (55)	34 (68)	45 (94)



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Kroenke et al. Arch Fam Med 1994; 3:774

Special Populations

- ★ Postpartum
- ★ Elderly
- ★ Medically ill
- ★ Children & adolescents



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Risk Factors

- ★ Childhood adversities
- ★ Current life events & stressors
- ★ Lack or loss of social support
- ★ Chronic medical illness
- ★ Family history ~ nature *and* nurture
- ★ Personality ~
insecure, worried, introverted, stress sensitive, obsessive, unassertive,
dependent
- ★ Postpartum ~ period of vulnerability
- ★ Menopause ~ no relationship to risk



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TABLE 9-12. Concordance rates for mood disorders in monozygotic and dizygotic twins

Study	Monozygotic twins		Dizygotic twins	
	Concordant pairs/total pairs	Concordance (%)	Concordant pairs/total pairs	Concordance (%)
Luxenberger 1930	3/4	75.0	0/13	0.0
Rosanoff et al. 1935	16/23	69.6	11/67	16.4
Slater 1953	4/7	57.1	4/17	23.5
Kallmann 1954	25/27	92.6	13/55	23.6
Harvald and Hauge 1965	10/15	66.7	2/40	5.0
Allen et al. 1974	5/15	33.3	0/34	0.0
Bertelsen 1979	32/55	58.2	9/52	17.3
Totals	95/146	65.1	39/278	14.0

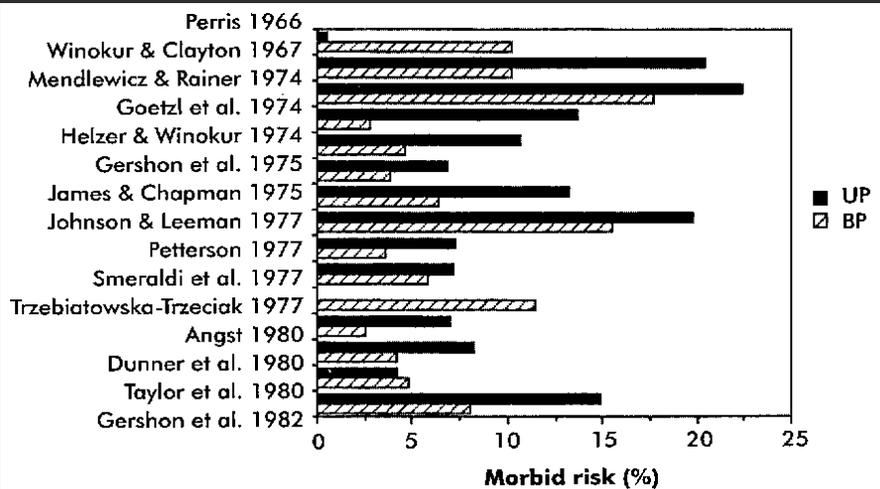
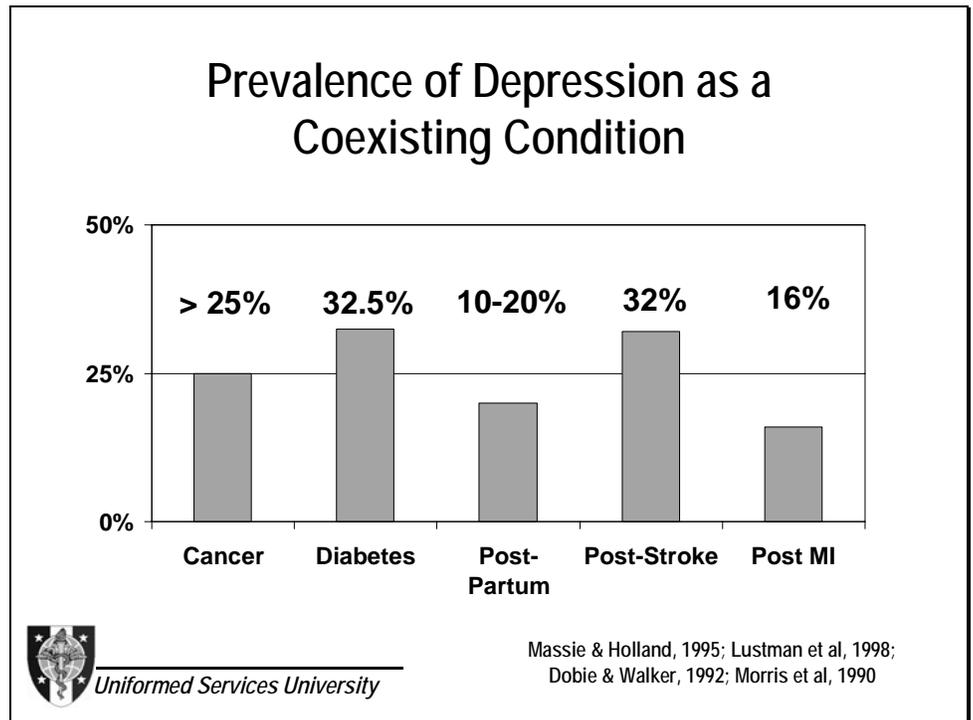
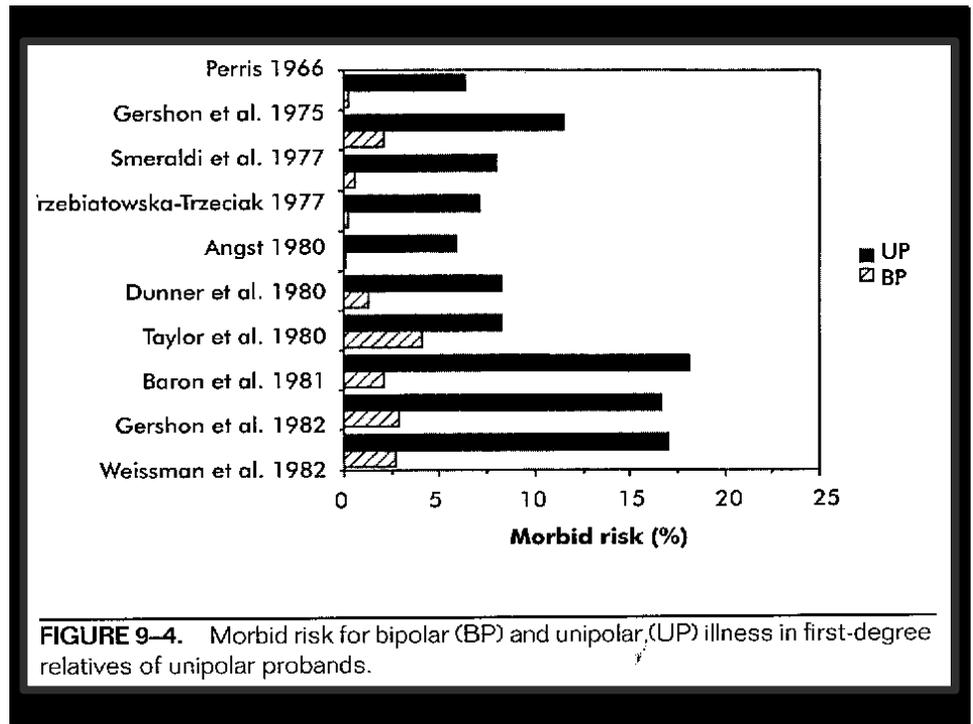


FIGURE 9-3. Morbid risk for bipolar (BP) and unipolar (UP) illness in first-degree relatives of bipolar probands.



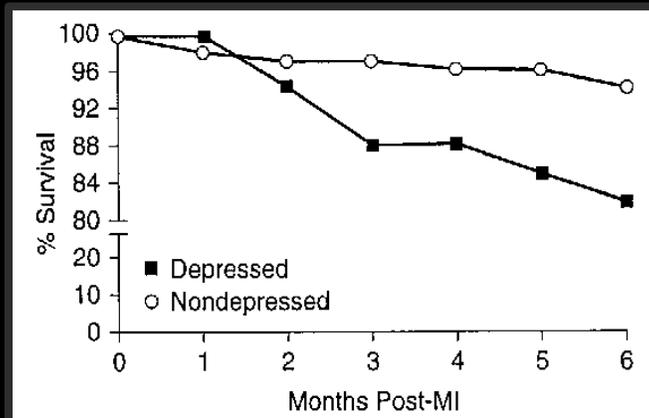


Figure 7-4. Mortality after myocardial infarction with and without comorbid depression. Reproduced with permission from Frasure-Smith N, Lesperance F, Talajic M: "Depression Following Myocardial Infarction: Impact on Six-Month Survival." *JAMA* 270:1819-1825, 1993. Copyrighted 1993, American Medical Association.

Table 7-9. Depressive Symptoms in Widows and Widowers Versus a Married Comparison Group*

	PERCENTAGE			
	2 Months (n = 350)	13 Months (n = 286)	25 Months (n = 274)	Married Comparison Group (n = 126)
Trouble sleeping	57	29	26	14
Feeling blue	40	25	17	2
Trouble concentrating	20	13	9	2
Poor appetite	19	8	6	0
Anhedonia	18	15	8	2
Thoughts of death/dying	15	11	10	1
Feelings of guilt	12	8	5	0
Feelings of worthlessness	8	6	6	0
Thoughts of ending life	2	3	1	0

*The widows and widowers have significantly higher percentages of each depressive symptom at each point in time than the comparison group.

Source: Adapted from Zisook S, Shuchter SR, Sledge PA, et al: "The Spectrum of Depressive Phenomena after Spousal Bereavement." *J Clin Psychiatry* 55 (suppl 4), 29-36, 1994. Copyright 1994, Physicians Postgraduate Press. Adapted by permission.

Table 7-7. DSM-IV-TR Classification of Mood Disorders (in DSM-IV-TR, Adjustment Disorder Constitutes a Separate Category)

DEPRESSIVE (UNIPOLAR) DISORDERS

Major Depressive Disorder

One or more major depressive episodes (i.e., at least 2 weeks of depressed mood or anhedonia and at least four other depressive symptoms)

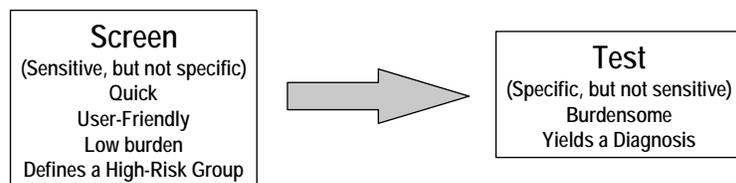
Dysthymic Disorder

At least 2 years of depressed mood along with associated symptoms, but without meeting the full criteria for major depressive episode (two rather than four additional symptoms)

DEPRESSIVE DISORDER NOT OTHERWISE SPECIFIED (NOS)

Getting an Efficient History

Use a Multi - Stage Sequence



PRIMary care Evaluation of Mental Disorders (PRIME-MD)*

During the PAST MONTH, have you OFTEN been bothered by...

- 1 ...little interest or pleasure in doing things?
- 2 ...feeling down, depressed, or hopeless?

* Spitzer RL, Williams JBW, Kroenke K, et al. JAMA 1994; 272:1749-1756.



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'The Five Minute Screening Interview'*

- ★ 'Have you been feeling SAD, BLUE, DOWN, or DEPRESSED?
- ★ 'Have you LOST INTEREST in, or get LESS PLEASURE from, the things you used to enjoy?

*Zimmerman, M. Diagnosing DSM-IV Psychiatric Disorders in Primary Care Settings: An Interview Guide For the Nonpsychiatrist Physician. Psych Products Press; 1994



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Major Depressive Disorder DSM-IV Diagnostic Criteria

- ★ Five or more symptoms (all day every day for at least two weeks)
- ★ Symptoms must include either ~
 - Depressed mood or
 - Diminished interest or pleasure in activities
- ★ Other symptoms ~
 - Significant weight loss or gain when not dieting
 - Insomnia or hypersomnia
 - Psychomotor retardation or agitation
 - Fatigue or loss of energy
 - Feelings of worthlessness or inappropriate guilt
 - Diminished ability to think or concentrate
 - Recurrent thoughts of death or suicidal ideation



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Symptoms of a Major Depressive Episode

- S sleep disturbance
- I loss of interest (anhedonia)
- G guilty ruminations
- E decreased energy
- C decreased concentration
- A altered appetite
- P psychomotor changes
- S suicidal (or morbid) ideation



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Always Assess Suicidality!

“Often people who are depressed have some troubling thoughts like they’d...

- ★ just as soon stay in bed or not wake up;
- ★ be better off dead; or
- ★ like to hurt or kill themselves

Ever have any thoughts like that? Tell me about them...”



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Suicide Assessment (Continued)

If the patient has ideas of suicide, ask them about:

- ★ A plan?
- ★ Feasibility of the plan?
- ★ Level of patient intent to carry out the plan?
- ★ Past history of attempts?
- ★ People who can support them?



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Table 21-3. Organic causes of depression.

<p>Medications</p> <p>Analgesics (eg, indomethacin, opiates)</p> <p>Antibiotics (eg, ampicillin)</p> <p>Antihypertensive agents (eg, propranolol, reserpine, α-methyldopa, clonidine)</p> <p>Antineoplastic agents (eg, cycloserine, vincristine, vinblastine)</p> <p>Cimetidine</p> <p>L-Dopa</p> <p>Insecticides</p> <p>Mercury, lead</p> <p>Oral contraceptives</p> <p>Sedative-hypnotics (eg, barbiturates, benzodiazepines, chloral hydrate, phenothiazines)</p> <p>Substances of abuse</p> <p>Alcohol</p> <p>Cocaine</p> <p>Opiates</p> <p>Neurologic disease</p> <p>Chronic subdural hematoma</p> <p>Dementias</p> <p>Huntington's disease</p> <p>Migraine headaches</p> <p>Multiple sclerosis</p> <p>Normal pressure hydrocephalus</p> <p>Parkinson's disease</p> <p>Strokes</p> <p>Temporal lobe epilepsy</p> <p>Wilson's disease</p> <p>Infectious disease</p> <p>Brucellosis</p> <p>Encephalitis</p> <p>HIV</p> <p>Infectious hepatitis</p> <p>Influenza</p> <p>Mononucleosis</p> <p>Subacute bacterial endocarditis</p> <p>Syphilis</p> <p>Tuberculosis</p> <p>Viral pneumonia</p>	<p>Neoplasms</p> <p>Bronchogenic carcinoma</p> <p>CNS tumors</p> <p>Disseminated carcinomatosis</p> <p>Lymphoma</p> <p>Pancreatic cancer</p> <p>Metabolic and endocrine disorders</p> <p>Addison's disease</p> <p>Anemia</p> <p>Apathetic hyperthyroidism</p> <p>Cushing's disease</p> <p>Diabetes</p> <p>Hepatic disease</p> <p>Hypokalemia</p> <p>Hyponatremia</p> <p>Hypoparathyroidism</p> <p>Hypopituitarism (Sheehan's disease)</p> <p>Hypothyroidism</p> <p>Pellagra</p> <p>Pernicious anemia</p> <p>Porphyria</p> <p>Thiamine, vitamin B₁₂, and folate deficiencies</p> <p>Uremia</p> <p>Collagen-vascular conditions</p> <p>Giant cell arteritis</p> <p>Rheumatoid arthritis</p> <p>Systemic lupus erythematosus</p> <p>Cardiovascular conditions</p> <p>Chronic heart failure</p> <p>Hypoxia</p> <p>Mitral valve prolapse</p> <p>Miscellaneous</p> <p>Chronic pyelonephritis</p> <p>Pancreatitis</p> <p>Peptic ulcer disease</p> <p>Postpartum depression</p>
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Major Depressive Disorder Subtypes

- ★ Melancholic features
- ★ Atypical features
- ★ With psychotic features
- ★ Seasonal Affective Disorder (SAD)
- ★ "Double depression"



TABLE 9–8. DSM-IV-TR diagnostic criteria for melancholic features specifier*Specify if:*

With Melancholic Features (can be applied to the current or most recent Major Depressive Episode in Major Depressive Disorder and to a Major Depressive Episode in Bipolar I or Bipolar II Disorder only if it is the most recent type of mood episode)

- A. Either of the following, occurring during the most severe period of the current episode:
- (1) loss of pleasure in all, or almost all, activities
 - (2) lack of reactivity to usually pleasurable stimuli (does not feel much better, even temporarily, when something good happens)
- B. Three (or more) of the following:
- (1) distinct quality of depressed mood (i.e., the depressed mood is experienced as distinctly different from the kind of feeling experienced after the death of a loved one)
 - (2) depression regularly worse in the morning
 - (3) early morning awakening (at least 2 hours before usual time of awakening)
 - (4) marked psychomotor retardation or agitation
 - (5) significant anorexia or weight loss
 - (6) excessive or inappropriate guilt

TABLE 9–9. DSM-IV-TR diagnostic criteria for atypical features specifier*Specify if:*

With Atypical Features (can be applied when these features predominate during the most recent 2 weeks of a current Major Depressive Episode in Major Depressive Disorder or in Bipolar I or Bipolar II Disorder when a current Major Depressive Episode is the most recent type of mood episode, or when these features predominate during the most recent 2 years of Dysthymic Disorder; if the Major Depressive Episode is not current, it applies if the feature predominates during any 2-week period)

- A. Mood reactivity (i.e., mood brightens in response to actual or potential positive events)
- B. Two (or more) of the following features:
- (1) significant weight gain or increase in appetite
 - (2) hypersomnia
 - (3) leaden paralysis (i.e., heavy, leaden feelings in arms or legs)
 - (4) long-standing pattern of interpersonal rejection sensitivity (not limited to episodes of mood disturbance) that results in significant social or occupational impairment
- C. Criteria are not met for With Melancholic Features or With Catatonic Features during the same episode.

TABLE 9-7. Types of major depressive episode

Mild: Few, if any, symptoms in excess of those required to make the diagnosis, and symptoms result in only minor impairment in occupational functioning or in usual social activities or relationships with others.

Moderate: Symptoms or functional impairment between “mild” and “severe.”

Severe, Without Psychotic Features: Several symptoms in excess of those required to make the diagnosis, and symptoms markedly interfere with occupational functioning or with usual social activities or relationships with others.

Severe, With Psychotic Features: Delusions or hallucinations. If possible, specify whether the psychotic features are mood congruent or mood incongruent.

Mood-congruent psychotic features: Delusions or hallucinations whose content is entirely consistent with the typical depressive themes of personal inadequacy, guilt, disease, nihilism, or deserved punishment.

Mood-incongruent psychotic features: Delusions or hallucinations whose content does not involve typical depressive themes of personal inadequacy, guilt, disease, death, nihilism or deserved punishment. Included are symptoms such as persecutory delusions (not directly related to depressive themes), thought insertion, thought broadcasting, and delusions of control.

Biological Markers

- ★ Depression is a clinical diagnosis
- ★ Dexamethasone suppression test
- ★ Thyroid releasing hormone
- ★ Neuroimaging studies
- ★ Functional imaging studies
- ★ Sleep studies



Pathogenesis Biological Theories

- ★ **Monoamines theories**
serotonin, norepinephrine, dopamine & related receptors
- ★ **Non-monoamine theories**
glucocorticoid, neurotrophic, excitatory amino acid, endocrine
- ★ **Global neurophysiologic theories**
dysregulation of circadian rhythms or neuronal electrolyte balance
- ★ **Neurophysiologic theories**
Prefrontal cortex, cingulate gyrus, basal ganglia, temporal lobes



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Pathogenesis Psychosocial Theories

- ★ **Loss and Grief**
- ★ **Psychoanalytic**
- ★ **Interpersonal**
- ★ **Cognitive**
- ★ **Learned helplessness**
- ★ **Behavioral**



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Treatment Options

- ★ Overall response rate ~ 85%
- ★ Psychotherapies
 - Cognitive-behavioral therapy (CBT)
 - Interpersonal therapy (IPT)
- ★ Antidepressant medications ~ SSRI, NRI, DNRI, SNRI, TCA, MAOI, stimulants, others
- ★ Other somatic therapies
 - Electroconvulsive Therapy (ECT)
 - Bright light therapy (“chronotherapy”)
 - Transcranial magnetic stimulation
 - Vagal nerve stimulation



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Recommendations for management of depression

1. A hopeful, optimistic tone should be established at the initial interview.
 - The severity of the depressive syndrome should be assessed, remembering that there may be individual and cultural differences in the way depression is experienced and expressed.
 - Extensive psychological probing should not be attempted when the patient is deeply depressed.
 - Suicidal risk should be determined initially and reassessed frequently.
2. Severe to moderate depression should be treated aggressively with somatic therapy.
 - Severely depressed or suicidal patients may require hospitalization.
 - Severely depressed outpatients may need frequent (e.g., twice-weekly) brief (e.g., 10- to 15-minute) contacts for support and medication management until their depression lifts.
 - Most patients will require at least 16–20 weeks of maintenance medication following an initial episode and thereafter should be given a trial of decreasing or discontinuing the medication. If symptoms reemerge, medication should be reinstated.
3. The clinician should determine whether psychosocial stressors are present that are contributing to the depressed mood and should counsel the patient on ways to cope with them.
4. Depressed patients tend to “get down” on themselves because they have been depressed; the clinician should help the patient learn to abandon negative or self-deprecating attitudes toward his or her depression through cognitive-behavioral therapy or other psychotherapeutic techniques.

Table 7-10. Typical Automatic Thoughts with Depression

<i>Automatic Thought</i>	<i>Definition</i>
Selective abstraction ("mental filter")	Drawing a conclusion based on only a small portion of the data
Arbitrary inference	Drawing a conclusion based on inadequate data or ignoring contradictory data
Absolutist ("all or none") thinking	Rigid dichotomies; patient is all good or all bad, perfect or completely flawed, a success or a total failure, etc.
Magnification and minimization	Overvaluing flaws, negative life events, or future bad outcomes, while undervaluing strengths, positive events, or potential good outcomes
Personalization	Taking blame or self-criticizing for events that are outside of one's control
Catastrophic thinking	Predicting the worst possible outcome while ignoring more likely events

Table 7-13. Adaptive and Maladaptive Schemas

<i>Adaptive Schemas</i>	<i>Maladaptive Schemas</i>
No matter what happens, I can manage somehow	I must be perfect to be accepted
If I can work at something, I can master it	If I choose to do something, I must succeed
I'm a survivor	I'm a fake
Others can trust me	Without a woman, I'm nothing
I'm lovable	I'm stupid
People respect me	No matter what I do, I won't succeed
I can figure things out	Others can't be trusted
If I prepare in advance, I usually do better	I never can be comfortable around others
I like to be challenged	If I make a mistake, I'll lose everything
There's not much that can scare me	The world is too frightening for me

Source: Reproduced with permission from Wright JH, Beck AT: "Cognitive Therapy." *American Psychiatric Press Textbook of Psychiatry*, 3rd Edition. Edited by Hales, RE, Yudofsky SC, Talbott JA. Washington, DC, American Psychiatric

Antidepressants By Presumed Mechanism of Action

MAO INHIBITORS

Irreversible Inhibitors of MAO-A and -B

- Phenelzine (Nardil)
- Tranylcypromine (Parnate)

Reversible Inhibitors of MAO-A (RIMAs)

- Moclobemide

TRICYCLIC ANTIDEPRESSANTS

Tertiary Amine Tricyclics

- Imipramine (Tofranil)
- Amitriptyline (Elavil)
- Doxepin (Sinequan)
- Trimipramine (Surmontil)
- Clomipramine (Anafranil)

Secondary Amine Tricyclics

- Desipramine (Norpramin)
- Nortriptyline (Pamelor)
- Protriptyline (Vivactil)
- Maprotiline (Ludionil)

SELECTIVE SEROTONIN REUPTAKE INHIBITORS (SSRIS):

- Fluoxetine (Prozac)
- Sertraline (Zoloft)
- Paroxetine (Paxil)
- Fluvoxamine (Luvox)
- Citalopram (Celexa)
- Escitalopram (Lexapro)

SELECTIVE NOREPINEPHRINE REUPTAKE INHIBITOR (NRI)

- Reboxetine (Vestra)

DOPAMINE-NOREPINEPHRINE REUPTAKE INHIBITOR (DNRI)

- Bupropion (Wellbutrin)

SEROTONIN-NOREPINEPHRINE REUPTAKE INHIBITOR (SNRI)

- Venlafaxine (Effexor)
- Duloxetine (Cymbalta)

SEROTONIN (5-HT₂) ANTAGONIST/REUPTAKE INHIBITORS

- Trazodone (Desyrel)
- Nefazodone (Serzone)

SEROTONIN (5-HT₂ AND 5-HT₃) ANTAGONIST AND ALPHA-2 ANTAGONIST

- Mirtazepine (Remeron)

SEROTONIN (5HT_{1A}) PARTIAL AGONIST

- Bupirone (BuSpar)

MONOAMINE RELEASING AGENTS ("STIMULANTS")

- Dextroamphetamine (Dexedrine)
- Methylphenidate (Ritalin, Concerta, Metadate)
- Pemoline (Cylert)
- Amphetamine Mixture (Adderall)

Table 21-5. Common clinical uses of antidepressants.

Major Indications	Secondary Indications
Major depressive disorder Dysthymia Bipolar disorder, depressed type Panic disorder (with or without agoraphobia)	Obsessive-compulsive disorder ¹ Generalized anxiety disorder Social phobia Bulimia nervosa Attention-deficit/hyperactivity disorder ² Diabetic polyneuropathy ¹ Chronic pain syndromes ¹ Sleep disorders Enuresis ³

¹ Mainly serotonergic antidepressants.

² Especially tricyclic antidepressants such as imipramine and desipramine.

³ Specific for the use of imipramine in children.

Table 21-10. Predictors of antidepressant response.

Positive Predictors	Negative Predictors
Vegetative symptoms (anorexia, weight loss, middle and late insomnia) Diurnal mood variation Psychomotor agitation or retardation Autonomous and pervasive symptoms Acute onset Family history of depression Dose of imipramine (or equivalent dose of another heterocyclic) above 125-150 mg/day Blood levels of desipramine (or imipramine and desipramine) above 200 ng/mL, and nortriptyline between 50 and 150 ng/mL	Coexistence of other significant psychiatric disturbances (particularly with hysterical or externalizing features) Chronic symptoms Psychotic features Hypochondriacal concerns or predominant somatic features Previous drug trial failure(s) History of sensitivity to adverse reactions

What Drug Should I Use? *Selecting an Agent*

- ★ Prior response (pt or family)
- ★ Side-effect profile
- ★ Age
- ★ Medical status
- ★ Medication interactions
- ★ Other psychiatric disorders
- ★ Cost
- ★ Patient preference



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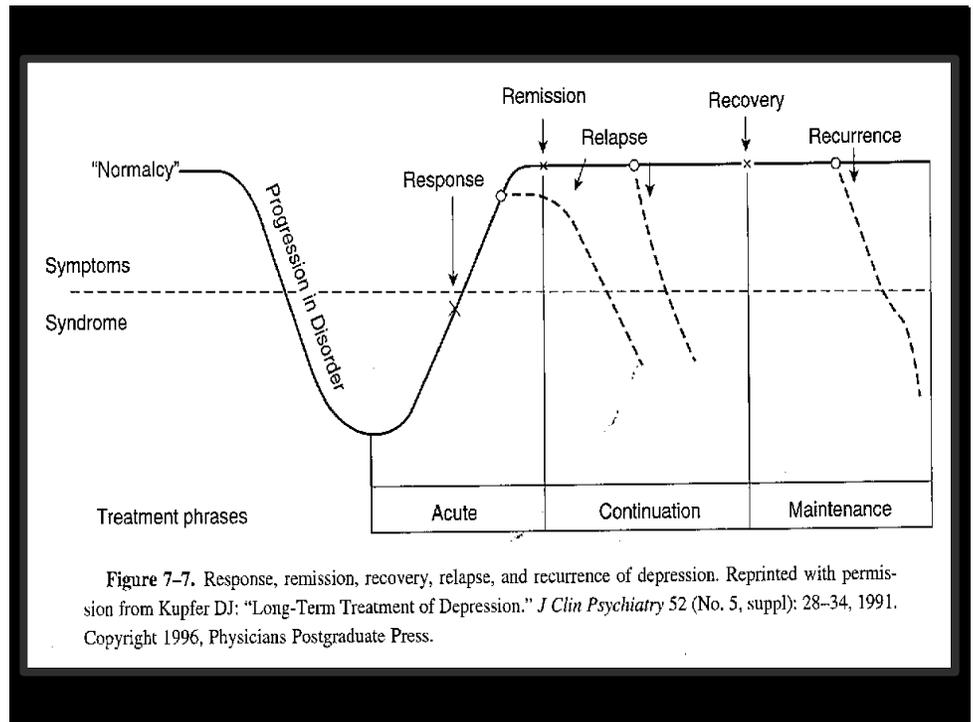


Table 7-17. Side Effects of Various Antidepressants, by Receptor Activity

<i>Receptor</i>	<i>Side Effects</i>
Histamine (H-1)	Sedation, weight gain, hypotension, delirium
Ach muscarinic	Dry mouth/eyes, blurred vision, urinary retention, constipation, memory impairment, delirium, resting tachycardia
Alpha-1	Orthostatic hypotension, reflex tachycardia, potentiation of anti-hypertensive effect of prazosin
Alpha-2	Block antihypertensive effect of clonidine, methyl dopa, guanfacine
5HT ₂	Anxiety, insomnia, ejaculatory dysfunction, hypotension
5HT ₃	Nausea, cramps, diarrhea

Table 7-19. SSRIs and the Cytochrome P450 System

<i>Isoenzyme</i>	<i>Inducers</i>	<i>Inhibitors</i>	<i>Main Drug Interactions</i>
1A2	Tobacco, charbroiled foods	Fluvoxamine, grapefruit juice, flavinoids, ciprofloxacin, norfloxacin	Theophylline, clozapine, haloperidol, olanzapine, propranolol, caffeine
2D6		Fluoxetine, paroxetine	Tricyclics, codeine
2C		Fluoxetine, fluvoxamine	Phenytoin, diazepam
3A4	Carbamazepine, phenobarbital	Nefazodone, fluoxetine, fluvoxamine, ketoconazole, cimetidine, erythromycin	Terfenadine, astemizole, cisapride, ziprasidone, carbamazepine, alprazolam, triazolam

Table 7-15. Comparison of Mechanism of Action of Different Antidepressants

<i>Mechanism</i>	<i>Tertiary TCA</i>	<i>Secondary TCA</i>	<i>SSRI</i>	<i>Bupropion</i>	<i>Venlafaxine</i>	<i>Nefazodone</i>	<i>Mirtazapine</i>
5HT uptake inhibition	<i>Yes</i>	No (slight)	<i>Yes</i>	No	<i>Yes</i>	<i>Yes</i>	No
5HT ₂ blockade	No (slight)	No	No	No	No	<i>Yes</i>	<i>Yes</i>
5HT ₃ blockade	No	No	No	No	No	No	<i>Yes</i>
NE uptake inhibition	<i>Yes</i>	<i>Yes</i>	No	<i>Yes</i>	<i>Yes</i>	No	No
Alpha-1 NE blockade	No (slight)	No	No	No	No	<i>Yes</i>	No
Alpha-2 NE blockade	No	No	No	No	No	No	<i>Yes</i>
Histamine-1 blockade	<i>Yes</i>	No	No	No	No	No	<i>Yes</i>
Acetylcholine blockade	<i>Yes</i>	<i>Yes (mild)</i>	No	No	No	No	No

Italics indicate clinically significant differences.

Adherence to Antidepressant Medication

Table 3. Factors Associated With Discontinuing Use of the Initial Antidepressant Medication Within 3 Months of Starting Treatment: Results of Multivariate Model*

Variable	Odds Ratio (95% Confidence Interval)
Communication factors reported by patients	
Told how long to continue with medication?	
≥6 mo	1.00 (Referent)
<6 mo	3.12 (1.21-8.07)
Duration not specified	1.02 (0.52-2.00)
Discussed adverse effects with physician during treatment?	
No	1.00 (Referent)
Yes	0.49 (0.25-0.95)
No adverse effect experienced	1.82 (0.78-4.24)
Adverse effects	
Experienced ≥ 1 moderately or extremely bothersome adverse effect?	
No	1.00 (Referent)
Yes	2.94 (1.51-5.71)
Clinical factors	
Depression symptoms were reported improved at 3 months?	
No	1.00 (Referent)
Yes	0.40 (0.20-0.82)
Had ≥3 office visits within 3 months?	
No	1.00 (Referent)
Yes	0.40 (0.19-0.82)
Marital status	
Married	1.00 (Referent)
Never married	1.74 (0.80-3.76)
Separated, divorced, or widowed	2.83 (1.49-5.39)

*Odds ratio and 95% confidence intervals compare the 79 patients who discontinued therapy with the 268 who continued it.

Table 21–12. Alternative therapies for treatment-resistant depression.^{1,2}

- Augmentation of TCAs or MAOIs with
 - Sleep deprivation [I]
 - Lithium [I]
 - Thyroid hormone [III]
 - L-Tryptophan [III]
 - Psychostimulants (amphetamine, methylphenidate)—in combination with TCAs only [III]
 - Carbamazepine [II]
- TCA/MAOI combination (use with extreme care) [II]
- ECT (reserved primarily for severe intractable depression or when the patient is acutely suicidal) [I]
- Phototherapy or light therapy [II]
- Psychostimulants alone (reserved largely for treatment in elderly depressed patients) [III]
- Psychotherapy (cognitive-behavioral and interpersonal psychotherapy) alone or in combination with TCAs [II]

¹ Modified and reproduced, with permission, from American Psychiatric Association: Practice guidelines for major depressive disorder in adults. *Am J Psychiatry* 1993;150(Suppl):4.

² [I] indicates recommended with substantial clinical confidence; [II] indicates recommended with moderate clinical confidence; [III] indicates options that may be recommended on the basis of individual circumstances. MAOI, monoamine oxidase inhibitor; TCA, tricyclic antidepressant.

Table 21–13. Relative contraindications to electroconvulsive therapy.

Conditions with increased intracranial pressure
Intracerebral hemorrhage
Pheochromocytoma
Recent myocardial infarction
Space-occupying intracerebral lesions (except for small, slow growing tumors without edema or other mass effect)
Unstable vascular aneurysms or malformations
