Current Comments

What Do We Know about Depression? Part 2: Diagnosis and Treatment

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This is the second part of a three part essay on depression. Last week, I discussed some models that have been proposed to explain the cause, or etiology, of this illness.[1] Researchers are divided according to whether they emphasize psychogenic or organic origins for depressive disorders. Only a few attempts have been made to integrate the knowledge generated by these viewpoints. This essay will examine the treatments for depression, and how they are related to the etiological models covered in Part 1.

From personal experience, I can say that depression is probably one of humanity's most insidious diseases. While it often happens suddenly, it more often may occur so gradually that the lay observer, indeed the biased relative or friend, cannot perceive that a disease process is taking place. It is so easy to rationalize that nothing "organic" is really wrong, and therefore with time and patience it will all go away. How then is one to recognize that we are dealing with an illness and not just a temporary phenomenon? Moreover, we are dealing with an enormous stigma associated with mental disorders that must in fact be communicated to the depressed patient as well. As is the case with death,[2] one doesn't like to face the reality or possibility of mental illness precisely because it is so intangible. I find this all the more inexplicable having heard from doctors and victims alike that the experience of depression is like no other. Can you imagine the pain that one experiences in depression, which is often so bad that only death can relieve it? Even many torture victims don't experience pain of such intensity that it drives them to suicide. Furthermore, since there are many suicides which are not accompanied by such pain, the unique feelings of the depressed are incomprehensible to most people. My own mother at about age 50 went into what was described as postmenopausal depression. It is an experience not easily forgotten—not even by the observer.[3] Unfortunately, many victims of depression hide the real depth of their pain. When suicide finally occurs, friends and family are taken completely by surprise.

In diagnosing depression, researchers and clinicians may choose from a number of objective criteria. That objective criteria are necessary cannot be disputed. For although there is general agreement on what the symptoms of depression are, they are numerous, and patients present a variety of symptom mixes. While a subjective feeling of being "depressed" is an important symptom, it is neither necessary nor sufficient for clinical diagnosis.[4] Without clinical guidelines, diagnosing depression would be more of an art than a science.[5]

Over the past two decades, a number of questionnaires were developed to diagnose depression and measure its severity. Some well-established questionnaires are the Minnesota Multiphasic

Personality Inventory,[6] the Hopkins Symptom Checklist,[7] the Zung Self-Rating Scale,[5] and the Beck Depression Inventory.[8] The use of the Beck Inventory, incidentally, is not restricted to those who subscribe to the cognitive model of depression. In Great Britain, the Maudsley Personality Inventory,[9] the Eysenck Personality Inventory,[10] and the Hamilton Rating Scale[11] are commonly used. And there are others.

These questionnaires typically present the patient with a series of statements. The patient indicates whether or not, or to what degree, the statements are true. Sample statements from the Beck Depression Inventory include, "I feel blue or sad," "I feel bored most of the time," "I am less interested in other people now than I used to be."[8] Variants of these statements appear in the other questionnaires as well. The patient's response to each statement is given a point value. The patient's total score is matched against a range of scores which determine the presence or severity of depression. Most psychological studies of depression identify their patient samples according to a mean score on one of the depression questionnaires mentioned here.

Recently, there have been impressive advances in developing physiological tests for depression. Most notable among them is the Dexamethasone Suppression Test (DST).[12] The test is similar to one used for years to diagnose Cushing's disease, a pituitary disorder. Patients are given a dose of dexamethasone. This steroid suppresses the production of cortisol, a hormone produced in the adrenal cortex. Normally, the level of cortisol in the blood should remain suppressed for about 24 hours. But patients with melancholia, roughly equivalent to what used to be called "endogenous" depression, often fail to remain cortisol-suppressed for that long.

The DST was first used experimentally to diagnose depression in the mid-1970s by Bernard Carroll and colleagues at the Mental Health Research Institute, University of Michigan.[13] Others have applied it since then but using differing levels of dexamethasone dosage, differing criteria for judging a melancholic response, and other procedural differences. This year, Carroll and colleagues published data from a six-year study which the authors claim provide an effective and standardized procedure for administering the DST.[12]

Patients diagnosed as depressed may receive some form of psychotherapy. The term psychotherapy can mean several things according to how strictly it is defined.[14] But it is commonly used to distinguish psychological treatments from physiological ones. It would be difficult to describe a typical course of psychotherapy for depression. Except for such examples as Beck's cognitive therapy and Lewinsohn's behavior therapy, which we shall discuss, it is rare to find descriptions of systematic procedures for treating depression with psychotherapy. Insights must be gained through numerous individual case studies dispersed throughout the literature.

The fact is that psychotherapy techniques differ among practitioners. Although therapists may have received training with a particular theoretical orientation, such as Freudian, Kleinian, or Myerian, they are typically flexible with their treatments. Many practice what Louis J. West, chairman of UCLA's department of psychology, calls "integrative psychotherapy," an eclectic approach which "suggests a willingness to pick and choose among theories and accept what seems to be useful in each, but without commitment to a single major theoretical position."[15] This approach involves applying knowledge from biochemistry, as well as from psychology, and it is common for practitioners to combine drug therapy with psychotherapy.[16] In choosing a treatment strategy for an individual patient, the therapist considers such variables as

severity of the depression, age of the patient, the risk of suicide, and other variables.[15]

One systematic approach to psychotherapy for depression is cognitive therapy, developed in the 1960s by Aaron T. Beck, University of Pennsylvania. Beck's etiological model views depression as resulting from a negative view of the self, the world, and the future. The depressed person perpetuates this outlook by systematically interpreting experiences in a negative way, even when alternative, more plausible explanations are available. The smallest failures are generalized as statements on the individual's worth. Even successes are construed negatively if the task performed was not done perfectly.[17]

Cognitive therapy is designed to replace a patient's faulty system of interpreting experience with a more reasonable way of looking at things. The therapist actively engages the patient, asking questions, suggesting alternative explanations for particular experiences. Cognitive therapy pays scant attention to distant childhood experiences. The emphasis is on the patient's present cognitions.[18]

The therapist usually meets with the patient twice a week at first, then once a week, so that a typical course of treatment consists of perhaps 20 sessions over a 15-week period. At these sessions, the therapist attempts to identify which "depressogenic" thought processes are at work. Richard Bedrosian and Beck have recently listed such processes, too numerous to fully list here, in the book *Psychotherapy Process*.[19] Some examples of these defective ways of thinking are: "selective abstraction," by which a person focuses on a negative detail out of context of the total experience; "arbitrary inference," by which a person arrives at negative conclusions on the basis of insufficient information; and "polarized thinking," by which a person categorizes all experiences as being either good or bad.[19]

More importantly than the mere identification of depressogenic thought processes, the therapist tries to get the patient to recognize these processes at work within himself or herself. Beck's *Cognitive Therapy of Depression* contains numerous examples of therapist/patient dialogues which illustrate how this might be done.[18]

Another method of psychotherapy for depression is practiced by the behaviorists. Behaviorists believe that depression arises when a person's behavior fails to elicit positive reinforcement.[20] The lack of reinforcement produces the symptoms of passivity and lethargy so often observed in depressives. Getting the depressed person to increase his or her activity level is a goal in itself.

Therapists may choose from a variety of behavior modification techniques in treating depression. One technique is to use high frequency behaviors to reinforce low ones. For a smoker, lighting a cigarette is a high frequency behavior. If a depressed person happens to be a smoker, he or she can be instructed to think about one item on a prepared list of positive thoughts before lighting each cigarette.[21] Carilyn Fuchs and Lynn Rehm, University of Pittsburgh, developed a six-week program which teaches depressives to reinforce themselves by allowing themselves something pleasant each time they engage in a nondepressive behavior, such as initiating a social interaction.[22]

Perhaps the most systematic behavioral treatment for depression has been developed by Peter M. Lewinsohn, University of Oregon. Lewinsohn incorporates a number of behavior modification techniques into a highly structured program of treatment.[20,23] The program includes several treatment innovations that Lewinsohn himself has introduced.

One of Lewinsohn's innovations is the use of weekly activity schedules. The patient examines a long list of "pleasant events" and rates each one according to which seems most or least pleasant. The

list includes such things as "watching people," "going to a restaurant," "learning to do something new," "laughing," "having a frank and open conversation," etc. From this list, the therapist and patient create a personalized schedule of nondepressive activities for the patient to perform.[24] Each time the patient engages in these nondepressive activities, he or she is credited with free therapy time.[20] Thus, an economic incentive helps to reinforce these activities. It should be mentioned that cognitive therapists use weekly activity schedules as part of their program. "In the early stages of cognitive therapy," writes Beck, "it is often necessary for the therapist to concentrate on restoring the patient's functioning to the premorbid level."[18]

Another of Lewinsohn's innovations is the use of home observations.[25] The therapist periodically visits the patient at home in order to observe his or her environment, including the people who live in the household. These visits can elicit important diagnostic information. Moreover, they involve a significant part of the patient's environment in the treatment process.

Is psychotherapy alone an effective treatment for depression? Not all depression, obviously. Depression is a heterogenous group of disorders, at least some of which are clearly somatic in origin. Psychotherapists claim success in treating what used to be called "reactive" depression, or non-somatic depression. But others are less certain. Hagop Akiskal, University of Tennessee, makes an analogy to hypertension: "Very mild hypertension can probably be treated with diet or exercise. But if the blood pressure is more sustained, you have to use medication. It's probably the same with depression. If it's mild, you can probably use psychotherapy. But the mere passage of time may remove the symptoms."[26] Akiskal acknowledges, however, that even when "physiological" treatments for depression are necessary, psychotherapy may improve coping skills and accelerate recovery.

Despite the various psychotherapies in use today, the fact is that more than half of all depressed patients receive antidepressive drugs.[27] Indeed, many clinicians who practice psychotherapy will often prescribe drugs. The most frequently prescribed antidepressants, the first line of treatment in many cases, are the tricyclics such as imipramine, marketed by Geigy under the trade name Tofranil. Imipramine, a dibenzazepine derivative, is manufactured by other firms as well.

The effectiveness of the tricyclics in treating many depressions has been widely documented, although it may take one to three weeks after the beginning of treatment before the patient notices any improvement.[27] The tricyclics work by enhancing the action of catecholamines, chemicals which are instrumental in the transmission of impulses from nerve cell to nerve cell. According to the catecholamine hypothesis, depression is caused by a depletion of catecholamines in the brain.[28] Recent studies on the mechanisms of tricyclic action suggest that the drugs diminish the sensitivity of the postsynaptic membrane, the "receiver" in impulse transmission, to changes in catecholamine levels.[29]

For a "typical" case of depression, a clinician might keep the patient on the full tricyclic dosage for a month after remission of symptoms. It is customary to keep the patient on a half dosage for six months thereafter.[27] The word remission is significant here, for it is not known how many depressions are actually cured by the drugs. While about 65 percent of those treated with tricyclics show definite improvement, the rate of relapse in the year following termination of treatment may be as high as 50 percent.[17] Many types of depression, especially those that used to be called "endogenous," are known to be recur-

rent. Some patients are maintained on antidepressant drugs indefinitely.

Tricyclics are a favored treatment in part because side effects seem to be mild. They include dry mouth and dizziness. However, the therapeutic dose-to-overdose ratio of tricyclics is low, and the possibility of lethal overdose is a cause of concern. In fact, some researchers believe that clinicians are so cautious in administering these drugs that they often prescribe an insufficient dosage. According to this view, tricyclics could help even more people if only they were given in greater doses.[27,30]

If the patient fails to respond to tricyclics, the clinician might consider another group of antidepressants, the monoamine-oxidase (MAO) inhibitors. Eutron, marketed by Abbott; and Parnate, by SmithKline and French, are MAO inhibitors. MAO is a substance that destroys catecholamines and serotonin after they have performed their functions in nerve transmission. Thus, to inhibit MAO is to enhance the action of catecholamines. However, one must exercise great caution with MAO inhibitors. MAO is found not only in the brain, but in other parts of the body as well. An MAO inhibitor will work on MAO in sites other than the brain. Patients who take MAO inhibitors can develop severe, even lethal, high blood pressure if they eat foods that contain the amino acid tyramine.[27] Such foods are common, and they include chocolate and aged cheese. Many MAO inhibitors have been removed from the US market.[27]

The drug lithium carbonate, which is neither a tricyclic nor an MAO inhibitor, is used for cases of manic-depression,[31] also called bipolar affective disorder. Bipolar illness is characterized by wild mood swings, from flights of impulsive excitement to deep melancholy. Recently, lithium has been shown to be effective in some cases of unipolar illness,[32] that is, depression without mania. This is especially true if the illness occurs in a family with a history of manic-depression. This leads researchers to believe that some unipolar disorders are the same entity as bipolar disorders with different symptoms.[33]

The effectiveness of lithium in treating bipolar affective disorder was first demonstrated in 1949 by John F. Cade, Victorian Department of Mental Hygiene, Australia.[31] But the drug did not become established throughout the Western world for many years. Perhaps the individual most responsible for the current popularity of lithium therapy is Mogens Schou, Aarhus University, Denmark.[34] His 1968 paper on lithium has received enough citations to rank as a classic.[35] Recently, the *Archives of General Psychiatry* devoted an entire special issue to lithium. That issue was dedicated to Schou.[36]

Although lithium therapy has proved a real benefit in treating manic-depression, clinicians often find it difficult to hold patients to a long-term program of therapy. Many patients discontinue the drug against the advice of physicians. One obvious reason for this is that lithium does have side effects, the most common of which is trembling hands.[37] But a study at the UCLA Affective Disorders Clinic by Kay R. Jamison, the clinic's director, and colleagues revealed some other reasons for patients' noncompliance. Many patients rebel against the idea that their moods are controlled by medication. Others who are in the depressive phase of their illness, for which lithium is somewhat less effective, believe that discontinuing the drug will elevate their moods.[38]

There is another reason why patients might discontinue their lithium. Some experience positive behavioral and cognitive changes when they are in their manic phase. Jamison and colleagues listed some of these positive experiences recently in the *American Journal of Psychiatry*.[39] They include increases in sensitivity and alertness, sexual intensity, productivity, creativity, and social

ease. The paper warns physicians to be aware that the manic-depressive on lithium may be fantasizing about lost "highs." "Effective therapy," the authors write, "must address the reality of the patient's positive perceptions of the illness as well as the altered state of perception induced by phases of the illness."[39]

Many aspects of antidepressant drug treatment have yet to be resolved. For example, there is no consensus on optimum dosages or frequency of administration. Choosing the right drug for the right patient is still a hit-or-miss affair, although progress is being made.[40] Nor is it known what effects, if any, these drugs will have if they are administered for many years.[41] Another subject of debate is prophylaxis, or the prevention of recurrences of depressive illness.[42] Perhaps most troubling of all are the preliminary results of a four-year study in progress by the National Institute of Mental Health, which showed that fully 40 percent of patients treated with imipramine or lithium never really recover from their depressive episodes.[43]

Again, many practitioners of psychotherapy recognize the usefulness of antidepressant medications and often treat patients with a mixture of psychotherapy and medicine. Cognitive therapists, for example, do prescribe tricyclics for patients who don't respond to cognitive therapy alone.[18] But Beck warns that total reliance on chemotherapy makes it less likely that patients will draw on their own coping mechanisms to deal with depression. "The relatively high relapse rates of patients previously treated with drugs..." he writes, "suggests that this contention may be valid."[18]

Other psychotherapists object to the strong emphasis placed by many researchers on the chemistry, rather than the psychology, of depression. Silvano Arieti, New York University Medical School, asserts, "In the several decades spent in psychiatric practice and research, I have never treated...a case of depression about which I could say there was no psychological factor involved. I have never seen a patient about whom I could say...that his depression came from nowhere and its origin had to be sought exclusively in metabolic disorder."[44] (p. 5)

If drugs or psychotherapy fail, clinicians may turn to electroconvulsive therapy (ECT), which I have discussed in a previous essay.[45] It appears that ECT is the quickest and most consistently effective treatment for depression.[46] Yet because of concern over possible side effects, which may include some degree of memory loss, many researchers describe ECT as a treatment of last resort. They recommend it for the most severe cases of depression, or when there is a real chance that a patient will commit suicide before antidepressant drugs can take effect. For such cases, there is nearly unanimous agreement that the benefits of ECT far outweigh any risks of side effects.[46]

Another treatment for depression now under investigation focuses on sleep abnormalities observed in depressed patients. In the early 1970s, David J. Kupfer, University of Pittsburgh School of Medicine, discovered that people diagnosed as having endogenous depression display abnormal rapid eye movement (REM) sleep patterns.[47] REM is that stage of sleep during which, it is believed, people dream. Rapid movement of the eyes characterizes this stage of sleep, hence the term rapid eye movement. The onset of REM occurs sooner in sleeping depressives than in nondepressed people. At first, researchers considered Kupfer's discovery significant because it provided a clinical marker for depression. But now Kupfer's results have taken on therapeutic significance.

Recently, Gerald Vogel and colleagues at Emory University have found

that depriving patients of REM sleep can help their depression.[48] This is done by simply awakening the sleeping patient whenever REM occurs. There are some peculiar aspects to this treatment. For one thing, it seems to work primarily for those depressions that respond to tricyclic drugs. For another, the treatment seems to have no effect until about three weeks after it is started, the same lag time as the tricyclic drugs. In fact, Vogel and colleagues theorize that the only reason tricyclic drugs work at all is that they deprive patients of REM sleep. The study of sleep patterns in depressed patients promises to be a fruitful area of research.

This essay has discussed some of the prevalent treatments for depression. But there are other treatments that lie outside of the mainstream. Orthomolecular medicine, for example, stresses healthful diets to treat illness and professes disdain for synthetic chemical medications. In psychiatry, orthomolecular therapists treat depressions with massive doses of vitamins. They also recommend "megavitamin therapy"[49] for schizophrenia, addictions, and criminal behavior. While researchers within the mainstream ignore this approach, they must realize that doubts about the effectiveness of psychotherapy, and concern over the safety of antidepressant drugs, make treatments like orthomolecular therapy attractive to many. The apparent safety and efficacy of Vogel's REM deprivation is encouraging. But medical researchers must continue their search for safe and effective treatments for what is a major medical problem.

Part 3 of this essay will discuss the problem of depression in adolescents.

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REFERENCES

1. **Garfield E.** What do we know about depression? Part 1. Etiology. *Current Contents* (19):5-12, 11 May 1981.
2. ----------. Death be not proud—meeting the needs of the dying through thanatology. *Current Contents* (12):5-13, 23 March 1981.
3. ----------. To remember my mother. *Current Contents* (30):5-6, 26 July 1976.*
4. **American Psychiatric Association, Task Force on Nomenclature and Statistics.** *Diagnostic and statistical manual of mental disorders.* Washington, DC: American Psychiatric Association, 1980. 494 p.
5. **Zung W W K & Durham N C.** From art to science: the diagnosis and treatment of depression. *Arch. Gen. Psychiat.* 29:328-37, 1973.
6. **Duckworth J.** *MMPI interpretation manual for counselors and clinicians.* Muncie, IN: Accelerated Development, 1979. 316 p.
7. **Lipman R S, Covi L & Shapiro A K.** The Hopkins Symptom Checklist. Factors derived from the HSCL-90. *J. Affect. Disorders* 1(1):9-24, 1979.
8. **Beck A T, Ward C H, Mendelson M, Mock J & Erbaugh J.** An inventory for measuring depression. *Arch. Gen. Psychiat.* 4:53-63, 1961.
9. **Garside R F, Kay S W K, Roy J R & Beamish P.** M.P.I. scores and symptoms of depression. *Brit. J. Psychiat.* 116:429-32, 1970.
10. **Kendall R E & DiScipio W J.** Eysenck Personality Inventory scores of patients with depressive illness. *Brit. J. Psychiat.* 114:767-70, 1968.
11. **Hamilton M.** A rating scale for depression. *J. Neurol. Neurosurg. Psychiat.* 23:56-62, 1960.
12. **Carroll B J, Feinberg M, Greden J F, Tarika J, Albala A A, Haskett R F, James N, Kronfol Z, Lohr N, Steiner M, de Vigne J P & Young E.** A specific laboratory test for the diagnosis of melancholia. Standardization, validation, and clinical utility. *Arch. Gen. Psychiat.* 38:15-22, 1981.
13. **Carroll B J, Curtis G C & Mendels J.** Neuroendocrine regulation in depression. II. Discrimination of depressed from nondepressed patients. *Arch. Gen. Psychiat.* 33:1051-8, 1976.
14. **Chaplin J P.** *Dictionary of psychology.* New York: Dell, 1975. 576 p.
15. **West L J.** Integrative psychotherapy of depressive illness. (Flach F F & Draghi S C, eds.) *The nature and treatment of depression.* New York: Wiley, 1975. p. 161-81.

16. **Weissman M M, Prusoff B A, Dimascio A, Neu C, Goklaney M & Klerman G L.** The efficacy of drugs and psychotherapy in the treatment of acute depressive episodes. *Amer. J. Psychiat.* 136:555-8, 1979.
17. **Beck A T & Rush A J.** Cognitive approaches to depression and suicide. (Serban G, ed.) *Cognitive defects in the development of mental illness.* New York: Brunner/Mazel, 1978. p. 235-57.
18. **Beck A T, Rush A J, Shaw B F & Emery G.** *Cognitive therapy of depression.* New York: Guilford Press, 1979. 425 p.
19. **Bedrosian R C & Beck A T.** Principles of cognitive therapy. (Mahoney M J, ed.) *Psychotherapy process.* New York: Plenum Press, 1980. p. 127-52.
20. **Lewinsohn P M.** The behavioral study and treatment of depression. (Hersen M, Eisler R M & Miller P M, eds.) *Progress in behavior modification.* New York: Academic Press, 1975. Vol. 1. p. 19-64.
21. **Seitz F C.** A behavior modification approach to depression: a case study. *Psychology* 8:58-63, 1971.
22. **Fuchs C Z & Rehm L P.** A self-control behavior therapy program for depression. *J. Consult. Clin. Psychol.* 45:206-15, 1977.
23. **Lewinsohn P M, Sullivan J M & Grosscup S J.** Changing reinforcing events: an approach to the treatment of depression. *Psychother./Theor. Res. Pract.* 17:322-34, 1980.
24. **Lewinsohn P M & Libet J.** Pleasant events, activity schedules, and depressions. *J. Abnormal Psychol.* 79:291-5, 1972.
25. **Lewinsohn P M & Shaffer M.** Use of home observations as an integral part of the treatment of depression: preliminary report and case studies. *J. Consult. Clin. Psychol.* 37:87-94, 1971.
26. **Akiskal H S.** Telephone communication. 5 March 1981.
27. **Prange A J.** Pharmacotherapy of depression. (Flach F F & Draghi S C, eds.) *The nature and treatment of depression.* New York: Wiley, 1975. p. 255-69.
28. **Schildkraut J J.** The catecholamine hypothesis of affective disorders: a review of supporting evidence. *Amer. J. Psychiat.* 122:509-22, 1965.
29. **Sulser F.** New cellular mechanisms of antidepressant drugs. (Fielding S & Effland R C, eds.) *New frontiers in psychotropic drug research.* Mount Kisco, NY: Futura, 1979. p. 29-50.
30. **Avery D & Winokur G.** The efficacy of electroconvulsive therapy and antidepressants in depression. *Biol. Psychiat.* 12:507-23, 1977.
31. **Cade J F J.** Lithium salts in the treatment of psychotic excitement. *Med. J. Australia* 36:349-52, 1949.
32. **Peet M & Coppen A.** Lithium treatment and prophylaxis in unipolar depression. *Psychosomatics* 21:303-13, 1980.
33. **Winokur G.** Is there a common genetic factor in bipolar and unipolar affective disorder? *Compr. Psychiat.* 21:460-8, 1980.
34. **Schou M.** Lithium in psychiatric therapy and prophylaxis. *J. Psychiat. Res.* 6:67-95, 1968.
35. ----------. *Citation Classic.* Lithium in psychiatric therapy and prophylaxis. *Current Contents/Clinical Practice* (38):12, 17 September 1979.
36. **Goodwin F K.** Introduction: the lithium ion. *Arch. Gen. Psychiat.* 36:833-4, 1979.
37. **Reisberg B & Gershon S.** Side effects associated with lithium therapy. *Arch. Gen. Psychiat.* 36:879-87, 1979.
38. **Jamison K R, Gerner R H & Goodwin F K.** Patient and physician attitudes toward lithium. *Arch. Gen. Psychiat.* 36:866-9, 1979.
39. **Jamison K R, Gerner R H, Hammen C & Padesky C.** Clouds and silver linings: positive experiences associated with primary affective disorders. *Amer. J. Psychiat.* 137:198-202, 1980.
40. **Stern S L, Rush A J & Mendels J.** Toward a rational pharmacotherapy of depression. *Amer. J. Psychiat.* 137:545-52, 1980.
41. **Kennedy P.** The use of psychiatric drugs for decades. *Brit. J. Psychiat.* 137:387-9, 1980.
42. **Helmchen H.** Current trends of research on antidepressive treatment and prophylaxis. *Compr. Psychiat.* 20:201-14, 1979.
43. **Sargent M.** Depression lingers among 40% of victims. *ADAMHA News* 5(18):1;4, 7 September 1979.
44. **Arieti S & Bemporad J.** *Severe and mild depression.* New York: Basic Books, 1978. 453 p.
45. **Garfield E.** Electroconvulsive therapy: malignant or maligned? *Current Contents* (42):5-9, 15 October 1979.
46. **Scovern A W & Kilmann P R.** Status of electroconvulsive therapy: review of the outcome literature. *Psychol. Bull.* 87:260-303, 1980.
47. **Kupfer D J.** REM latency: a psychobiologic marker for primary depressive disease. *Biol. Psychiat.* 11:159-74, 1976.
48. **Vogel G W, Vogel F, McAbee R S & Thurmond A J.** Improvement of depression by REM sleep deprivation. *Arch. Gen. Psychiat.* 37:247-53, 1980.
49. **Hoffer A.** Megavitamin therapy. (Herink R, ed.) *The psychotherapy handbook.* New York: New American Library, 1980. p. 370-4.

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