. . . a review of the literature—1960—1970

part II. sleep studies

Richard Wyatt,
Benedict A. Termini, and John Davis

Similarities among dreams, hallucinations, and primary process thinking are often compared. Based on earlier ideas of William James and Hughlings Jackson, Feinberg and Evarts (1969) recently formulated three hypotheses associating dreams and hallucinations:

- Neurophysiological processes associated with dreams in the sleeping state are also associated with hallucinations in the waking state.
- Those mechanisms involved in the perception of visual hallucinations and dreams are the same mechanisms which underly normal vision.
- Dreams and hallucinations result from the elimination of an inhibitory process.

Since hallucinations are one of the most striking characteristics of some forms of schizophrenia, it is not surprising that considerable effort has gone into studying the physiology of sleep in schizophrenic patients. The most important stimulus for these efforts was the observation that there are periodic episodes of rapid eye movements (REM) during sleep (Aserinsky and Kleitman, 1953) and that these REM periods are highly correlated with dream reports (Aserinsky and Kleitman, 1955, and Dement and Kleitman, 1957). Normally, REM sleep alternates with the rest of sleep (nonREM sleep) in 90-minute cycles and occupies 20–25 percent of total sleep.

In an important series of experiments aimed at delineating a function for REM sleep, subjects were intentionally deprived of REM sleep for periods lasting from several days to over 1 year. This deprival was accomplished by either awakening a subject every time a REM period began (as evidenced by EEG tracings) or by giving him one of the many psychoactive drugs which suppress REM sleep. When the subject was once again permitted to have REM sleep (regardless of which method of REM deprivation had been used), REM sleep periods took up a higher proportion of the night than they had during baseline (preREM-deprivation) observations. This finding suggested a hydraulic model of REM sleep—i.e., that during REM deprivation the brain was capable of storing some "neurohormone" which discharged during the period of REM rebound (Dement and Fisher, 1963)—which, in turn, suggested that this increased REM pressure might tend to dissipate itself in a pathological manner (e.g., hallucinations) during waking hours.

While initial reports indicated that REM deprivation in normal subjects (Dement, 1960; Dement and Fisher, 1963; and Sampson, 1966) produced heightened anxiety, irritability, and difficulty in concentrating, subsequent better controlled experiments (Dement, 1964; Kales et al., 1964; and Dement, 1966) failed to produce gross psychological changes, although relatively subtle deviations were sometimes noted. Furthermore, no significant adverse effects were noted in a series of patients with depression (Wyatt et al., 1971) or narcolepsy (Wyatt, Fram, and Snyder, 1970) who had received phenelzine (a monoamine oxidase inhibitor which induces REM deprivation) for as long as a year. Because it seems unlikely that the brain could retain a constantly built-up "neurohormone" for a year, these findings tend to discredit the hydraulic model of REM sleep; nonetheless, this model has been an important impetus for many studies of schizophrenic sleep.

Some investigators have hypothesized that, if schizophrenic patients were found to have an abnormally high amount of REM sleep (Fisher and Dement, 1963), a corresponding tendency might exist for REM to manifest itself in some manner during waking hours (Rechtschaffen, Schulsinger, and Mednick, 1964). Most studies of chronic schizophrenic patients have not, however, demonstrated marked deviations from normal in amount of REM sleep (Dement, 1955; Koresko, Snyder, and Feinberg, 1963; Feinberg et al., 1964; Feinberg, Koresko,

and Gottlieb 1965; and Traub, 1970). While a number of investigators have noted markedly lower than normal amounts of slow-wave sleep in schizophrenic subjects (Caldwell and Domino, 1967; Caldwell, 1969; Feinberg, 1967 and 1969; Feinberg et al., 1969; and Kunugi, 1970, this finding's significance is unclear since depressed patients (Mendels and Hawkins, in press), some mental retardates (Feinberg, Braun, and Shulman, 1969), chronic brain syndrome patients (Feinberg, 1967), the normal elderly (Feinberg, Koresko, and Heller, 1967), and students under stress (Lester, Burch, and Dossett, 1967) also have decreased slow-wave sleep.

Two studies of chronic schizophrenic patients have shown contrasting abnormalities in amounts of REM sleep. Gulevich, Dement, and Zarcone (1967) found an *increased* amount of REM sleep in 13 chronic, nonmedicated, remitted schizophrenic patients, as compared to seven nonpsychotic controls, while Azumi (1966) demonstrated that REM time was *lower* in a group of 35 chronic, nonmedicated schizophrenics than in 33 normals. It seems probable that Azumi's chronic patients were more actively ill than those in the Gulevich group's study and possible that acutely ill schizophrenic patients might have even lower amounts of REM sleep. This possibility is supported by a study which revealed that short-term schizophrenic patients had significantly lower values for emergent stage 1 EEG ("REM time") and REM than did long-term patients (Feinberg et al., 1964). Abnormally low amounts of REM sleep were also seen in a study in which the sleep of six acute schizophrenic patients was monitored nightly during 10 psychotic episodes occurring over many months (Kupfer et al., 1970). The patients' behavior was monitored during this period, and each psychotic episode was divided into a waxing and waning phase. In the waxing phase of the illness, there was a decrease in both REM and nonREM sleep; the REM decrease, however, was proportionately greater than the nonREM decrease and lagged behind nonREM in returning to normal during the waning phase of the illness. The absence of a subsequent REM rebound in these patients was a surprising finding, particularly since psychotically depressed patients with similar REM deficits evidence very large REM rebounds upon recovery (Snyder, 1969). Marked decreases in the amount of REM sleep have also been noted in smaller, less comprehensive studies of acute schizophrenics (Lairy, 1966; Lairy et al., 1965; and Stern et al., 1969); Vincent et al. (1968) did not observe any REM deficits in schizophrenics monitored with telemetry.

Studies by Zarcone et al. (1968), Zarcone and Dement (1969), and Azumi et al. (1967) support previous naturalistic observations that active chronic schizophrenic patients do not evidence compensatory REM increases following experimental periods of REM deprivation (although Zarcone et al. did observe greater than normal REM rebound in *remitted* schizophrenic patients). In the one study in which chronic patients *did* show compensatory REM increases (Vogel and Traub, 1968), REM deprivation had been accomplished by the use of amphetamine, a drug which suppresses REM sleep but is also associated with large REM rebounds when its use is discontinued. Moreover, the chronic schizophrenics in this study lacked florid symptomatology and may have been more similar to Zarcone et al.'s remitted patients than to their active patients. In none of these studies was there an increase in patient symptomatology during REM deprivation.

A recent study by Wyatt et al. (1970) suggests that schizophrenia may be characterized by a breakdown in the normal boundaries between the REM-sleep and waking states. These investigators report that spontaneous palmar skin potential fluctuations in seven of eight nonmedicated acute schizophrenics were more frequent in REM sleep than in other stages of sleep and equal in frequency to waking values. By contrast, normal controls showed a marked decrease in skin potential fluctuations during REM sleep. Since studies of cats have demonstrated that the skin potential is actively inhibited during REM sleep, the frequent fluctuations noted during the REM sleep of these acute schizophrenic subjects may represent a failure of normal inhibitory processes. The recent finding that autistic children's evoked potential amplitudes are *increased* (rather than decreased as is normally the case) during REM sleep

has been similarly interpreted (Ornitz et al., 1968).

A series of animal and human pharmacological studies have suggested a model which may ultimately prove more useful for explaining REM abnormalities in schizophrenia than the previously discussed hydraulic model. This alternative model stems from recent investigations of parachlorophenylalanine (PCPA), an inhibitor of tryptophan hydroxylase (the rate-limiting enzyme in serotonin synthesis). When Dement et al. (1969) administered PCPA to cats, monophasic sharp waves (which normally occur almost exclusively in REM sleep) were produced in both nonREM-sleep and waking states. Because of their spike-like appearance and location in the pons, geniculate, and occipital regions, these sharp waves are referred to as PGO spikes. Along with PGO spiking, daily PCPA administration was associated with a marked diminution of both REM and nonREM sleep and with aberrant behavior in the waking state—rage, hypersexuality, hyperphagia, and activity reminiscent of humans undergoing hallucinations. Attempting to explain these responses to PCPA, Dement et al. postulated that the PGO spikes acted as internal stimuli which were too disturbing to allow the cats to sleep. These investigators also considered the PGO spiking responsible for the production of "hallucinatory" behavior in the cats. The diminution of REM and nonREM sleep associated with PCPA administration tended to be a relatively transitory phenomenon, for REM and nonREM sleep time generally returned to normal levels after approximately 1 week of diminution.[1] PCPA-induced abnormalities in behavior and PGO spiking, however, continued unabated. After administration of either 5-hydroxytryptophan (which bypasses the PCPA enzymatic block) or chlorpromazine all PCPA-induced changes were reversed.

Data also exist on the effects of PCPA in man. Recently, Wyatt (1970) and his associates (1969) reported on the sleep of 11 patients who had been given PCPA for its possible therapeutic effects. While the decrease in nonREM sleep seen in cats did not occur, all 11 patients showed diminished REM sleep over a 2–3-week period. When the drug was discontinued, REM required over 3 weeks to return to normal levels. Again, compensatory increases in REM sleep time did not occur in the period following PCPA-induced REM deprivation. For this reason, it was concluded that PCPA irreversibly blocks tryptophan hydroxylase in human brain, resulting in a decrease in the synthesis of serotonin (believed to play a fundamental role in REM production). Supporting this interpretation was the finding that, when the enzymatic block was bypassed by oral administration of 5-hydroxytryptophan, REM sleep returned to normal levels. Because possible methods for measuring the presence of PGO spikes in man have only recently been proposed (Wilson and Nashold, 1969; Pivik and Dement, 1970; and Rechtschaffen et al., 1970), they have not yet been used with patients receiving PCPA; hopefully, data on this subject will become available in the near future.

The psychological effects of PCPA administration in man are unclear. In an early study, PCPA (in a dose up to 3 g./24 hr.) was given to prisoner volunteers without significant psychological effects (Cremata and Koe, 1966). When PCPA was later administered to patients with carcinoid tumor (4 g./24 hr.), however, such psychological symptoms as depression, confusion, hallucinations, and anxiety were present in four out of five subjects (Engelman, Lovenberg, and Sjoerdsma, 1967). Subsequently, in a more careful, double-blind study of seven patients with carcinoid tumor, behavioral changes (as measured by a psychiatric interview and rating scale) were significantly correlated with the period of highest PCPA dosage (Carpenter, 1970). The behavioral changes noted in this study included depression, anxiety, restlessness, irritability, crying, agitation, withdrawal, and lack of interest. The fact that maximum PCPA dosage was generally smaller than in the earlier study of carcinoid patients and that particularly labile patients were not given the drug may explain the absence of hallucinations or clear delusions in these patients. It is possible that higher amounts of PCPA

[1] It is interesting to note that the cats, like the REM-deprived schizophrenics discussed on p. 46, did *not* evidence REM rebound in the period following PCPA-induced REM deprivation.

might have produced effects similar to those seen in cats who received PCPA in amounts greater than 50 mg./kg./day (the highest dosage of PCPA that has yet been administered to man).

If schizophrenics are characterized by a deficiency in serotonin metabolism, as predicted by the sleep studies, it does not necessarily follow that these patients must have low brain serotonin concentrations. An hypothesis concerning the mechanism of action of LSD, for example, suggests that this hallucinogen blocks serotonin receptor sites, thereby increasing brain serotonin concentrations (through a feedback mechanism) and decreasing concentrations of serotonin's metabolite, 5-hydroxyindoleacetic acid (5HIAA) (Aghajanian, Foote, and Sheard, 1968). Smythies, Benington, and Morin (1969) have also speculated about the blocking of serotonin receptors by hallucinogenic drugs. Thus, depending on its cause, a *functional deficiency in serotonin metabolism* could be associated with either an absolute increase or decrease in brain concentrations of serotonin or its metabolites. Symptomatic of the uncertainty surrounding this subject is the fact that Woolley, who initially postulated a serotonin deficit in schizophrenia (Woolley and Shaw, 1954), later reversed himself and predicted a serotonin excess in this disorder (Woolley, 1962).

The results of studies of serotonin concentrations in schizophrenia are not uniform, and, of course, these levels can only be measured peripherally. Feldstein, Hoagland, and Freeman (1959) found no differences between chronic schizophrenic and normal blood serotonin concentrations, although low concentrations were noted in acute psychotic patients. By contrast, Jus, Laskowska, and Zimmy (1958) reported low blood serotonin concentrations in chronic schizophrenics. Ljungberg (1963) observed higher urinary 5HIAA concentrations in patients with "fatal catatonia" than in other psychotics, and Banerjee and Agarwal (1958) found high urinary 5HIAA concentrations in schizophrenics. These findings must be contrasted with those of Buscaino and Stefanachi (1957) who noted low urinary 5HIAA concentrations in schizophrenics, of Leyton (1958) who reported urinary 5HIAA excretion to be low in 20 percent of the schizophrenic patients he examined, and of Fragoso Mendes and Lopes do Rosario (1959) who found no difference in urinary 5HIAA between normals and schizophrenics.

To test the possibility that schizophrenics are unable to synthesize adequate amounts of serotonin, Lauer et al. (1958) administered tryptophan to both schizophrenic patients and normal control subjects. While they found no increase in 5HIAA excretion in the schizophrenic urine, there was a 100 percent increase of 5HIAA in the urine of normals. Neither Kopin (1959) nor Shaw, Lucas, and Rabinovitch (1959) were able to confirm this finding in their respective studies of adult and childhood schizophrenics. More recently, Christodoulou and Papaevangelou (1966) found no difference in the urinary 5HIAA excretion of schizophrenic and normal subjects to whom they had administered diets high in protein and carbohydrate.

In studies more closely related to brain function, Bowers, Heninger, and Gerbode (1969), Ashcroft et al. (1966), and Chase, Schnur, and Gordon (1970) found lower 5HIAA cerebrospinal fluid concentrations in schizophrenic patients than in either neurological patients or normal controls. Persson and Roos (1969), however, found no difference between schizophrenic and normal 5HIAA concentrations. In each of these studies, psychoactive drugs were administered within a few days of the 5HIAA determination, and the effect of these drugs is not clear (Chase, Schnur, and Gordon, 1970).

Attempts to treat schizophrenia with serotonin or its precursor, 5-hydroxytryptophan, have been generally unsuccessful (Woolley, 1962; Klee et al., 1961; Hoagland, 1958; and Pollin, Cardon, and Kety (1961). However, both Sherwood (1955), who injected 15–75 ug. (2–3/wk.) of serotonin intraventricularly to four chronic schizophrenics, and Ljungberg (1963), who gave unspecified dosages of 5-hydroxytryptophan to nine "fatal catatonics," reported "great improvement" in the patients they had studied.

Studies of serotonin deficits in schizophrenia are subject to the same general criticisms that have been directed to investigations of other

possible biochemical defects in schizophrenia —i.e., failure to adequately control for experimental biases related to such factors as diet, drugs, and hospitalization. Thus far, the serotonin hypothesis—like so many others—has not been consistently supported by experimental evidence.

Summary (Part 2)

Because of obvious parallels between dreams and hallucinations, the physiology of sleep in schizophrenic patients has evoked substantial investigative interest. Particular attention has been directed to possible abnormalities of rapid-eye-movement (REM) sleep—periodic episodes which are highly correlated with dreaming and which usually occupy 20–25 percent of total sleep time. Although most studies of chronic schizophrenics have not found marked abnormalities in amount of REM sleep, both *acute* and *actively symptomatic chronic* patients reportedly evidence lower than normal amounts of REM sleep. Thus, decreased REM sleep appears to be associated with the waxing phase of the schizophrenic disorder. But since experimentally induced REM deprivation has generally failed to produce gross adverse psychological effects in normal subjects, the significance of this finding is unclear. Another unusual characteristic of actively ill schizophrenics is their failure to evidence compensatory increases in REM sleep time (REM rebound) following periods of REM deprivation. Various theories have been offered as explanations for these and other abnormalities in the sleep of schizophrenics—the two most important being the hydraulic model of REM sleep and the REM-sleep/serotonin-deficit hypothesis. Thus far, however, none of these theories has been consistently supported by experimental evidence.

Conclusion

This review has focused on several major areas of the biochemical investigation of schizophrenia. How many of these areas focus on postulated aberrations of biogenic amines is immediately apparent. The Frohman factor, for example, is thought to alter red-cell uptake of amines, and the physiological sleep abnormalities which characterize acute schizophrenia have been induced in both animals and man by manipulating brain serotonin concentrations. This focus of interest is not surprising since, when we look at our academic psychiatric centers, a very large percentage of biological researchers are studying one or another aspect of biogenic amines. Whether this convergence of interest will prove to be of practical importance in the prevention and treatment of schizophrenia remains to be seen.

The transmethylation hypothesis of schizophrenia has excited considerable investigative interest and has generally been studied using the "precursor-load" strategy. Both methionine and betaine seem to make schizophrenic patients more psychotic, but because toxic and schizophrenic psychoses have not been clearly differentiated, the significance of this psychotic worsening is difficult to assess. Furthermore, although methionine loading has increased brain concentrations of S-adenosylmethionine (the putative methyl donor) in rats (Baldessarini, 1967), no such increases have yet been found following methionine loading in man. Given the schizophrenic's postulated "abnormal" ability to form, or inability to metabolize, methylated substances, methionine loading should theoretically cause differential reactions in schizophrenic and nonschizophrenic subjects; but since the methionine precursor-load strategy has only twice been carried out in nonschizophrenic subjects (Alexander et al., 1963), this important aspect of the transmethylation hypothesis cannot be meaningfully evaluated.

On the grounds that they are methyl acceptors which theoretically should lower brain concentrations of aberrant methylated substances, nicotinic acid and NAD have been used to treat schizophrenics for almost 20 years. Nevertheless, no evidence exists that nicotinic acid or NAD, in fact, perform this function in man, and current evidence of their therapeutic efficacy in schizophrenia is, at best, equivocal.

During the last 8 years, DMPEA (or "pink spot") has attracted as much worldwide attention as most of the other biochemical substances in the study of schizophrenia com-

bined. This interest probably stems from Osmond and Smythies' (1952) identification of DMPEA as a possibly provocative compound with regard to the transmethylation hypothesis. Over the years, the study of DMPEA has been plagued by repeated failures of one investigator to replicate another's experiments—failures which, for the most part, appear to result from inadequate biochemical methodology leading to type A, B, and C errors (see figure 1 and the discussion on pp. 11–12). DMPEA's presence in urine has been demonstrated through mass spectrometry (Stabenau, Creveling, and Daly, 1970), but whether it is formed in the body or is obtained from preformed plant foods (e.g., tea) is not yet clear. The fact that DMPEA's presence in or absence from the urine correlates with the addition or removal, respectively, of tea from the diet of normal subjects is suggestive but not conclusive evidence that tea is the source of DMPEA in schizophrenics. It is also possible that DMPEA occurs in one particular subgroup of schizophrenics (e.g., acute schizophrenics) but is generally absent from other types of schizophrenics.

First described 10 years ago, the "mauve factor" now appears to be a group of substances (including a pyrrole derivative). Neither its significance to schizophrenia's etiology nor its differential occurrence in schizophrenics, as opposed to normals, has been established.

Studies of bufotenine, like those of DMPEA, have suffered from inadequate biochemical methodology and either poor or nonexistent controls. While the recent finding in human brain of an enzyme capable of N-methylating serotonin to bufotenine (Mandell and Morgan, 1970) is presumptive evidence of bufotenine's existence in man, and while it may be present in greater concentrations in schizophrenics than normals (Sireix and Marini, 1969, and Fischer and Spatz, 1970), conclusive evidence of bufotenine's hallucinogenic properties in man has yet to be brought forward. Since bufotenine probably does not cross the blood brain barrier, its role in schizophrenia will be hard to demonstrate.

One of the most consistent findings in the biochemical investigation of schizophrenia has been that there is some abnormality in the schizophrenic's ability to handle histamine. It is therefore surprising that only four studies of the histamine-schizophrenia relationship have been carried out in the last 10 years. A possible explanation for this neglect is the fact that, although histamine is in part metabolized by methylation, none of its metabolites are considered hallucinogenic, which, of course, does not jibe with the widely accepted transmethylation hypothesis. Only recently, in fact, has *any* theoretical hypothesis about histamine's relationship to schizophrenia been formulated (Cowen, 1969, and Pfeiffer et al., 1970).

Studies of taraxein, serum factors, and other substances thought to be involved in immune systems have presented a confusing array of results, most of which have not been replicated in experiments carried out by researchers other than the original investigator. This failure to replicate may stem from the complexity of immunological systems and protein chemistry and from psychiatric researchers' general unfamiliarity with them. Until independent investigators are able to consistently replicate each other's findings, the importance of taraxein and comparable substances will remain in doubt.

Although there is considerable evidence of the Frohman factor's presence in schizophrenic patients, its chemical structure and function remain an open question. Recently, Ryan et al. (1968) found a substance in the plasma of nonschizophrenic, chronically hospitalized patients which was quite comparable to that found in schizophrenic patients (i.e., the Frohman factor) but different from that found in normal controls. From their study, it appears that some correlate of hospitalization—rather than schizophrenia, per se—may produce the Frohman factor.

Most of the better known and established biochemical views of schizophrenia are discussed above, but new areas of interest are constantly developing and old ones reopening. Three suggestive new findings, for example, are that the sex of the fetus may determine the presence of puerperal psychosis (Taylor and Levine, 1969), that hexenoic acid is present in the sweat of schizophrenics (Smith, Thompson,

and Koster, 1969) and that 6-hydroxydopamine may be formed by schizophrenics (Stein and Wise, 1971). The generalized theory that excessive or deficient concentrations of substances normally present in the human body (i.e., the "orthomolecular theory") are involved in the schizophrenic process (Pauling, 1968) is an organizational research strategy frequently applied to schizophrenia.

While it is relatively new and untested, the REM-sleep/functional serotonin-deficit theory is promising in that it combines data from physiology and biochemistry, provides an animal model, proposes a functional relationship between dreams and hallucinations, and can be used in conjunction with other hypotheses involving a disturbance of serotonin metabolism. Despite this theory's attractiveness, no adequately controlled studies have demonstrated differences between schizophrenic and normal serotonin metabolism and no properly controlled study has shown clinical improvement in schizophrenic patients in whom serotonin concentrations have been elevated.

The biochemical investigation of schizophrenia has been hampered by the complex, inaccessible nature of the brain. To date, peripheral tissue examination has not unlocked secrets of practical importance to schizophrenia, and attempts at direct examination of the brain have not yet been successful. The discovery of enzyme defects in diseases of glycogen storage, amino aciduria, and lipid storage affecting the brain points toward more rewarding findings to come. Moreover, research methodology is constantly improving, and this, too, will aid in our further investigative efforts.

References

Acebal, E.M., and Spatz, H. Effect of trifluperidol (R 2498) on the urinary elimination of bufotenin in schizophrenia. *International Journal of Neuropsychiatry,* 3:472–476, 1967.

Aghajanian, G.; Foote, W.E.; and Sheard, M.H. Lysergic acid diethylamide: Sensitive neuronal units in the midbrain raphe. *Science,* 161(3842):706–708, 1968.

Alexander, F.; Curtis, G.C., III; Sprince, H.; and Crosley, A.P., Jr. L-methionine and L-tryptophan feedings in non-psychotic and schizophrenic patients with and without tranylcypromine. *The Journal of Nervous and Mental Disease,* 137(2):135–142, 1963.

Ananth, J; Ban, T.A.; Lehmann, H.E.; and Bennett, J. Nicotinic acid in the prevention and treatment of artificially induced exacerbation of psychopathology in schizophrenics. *Canadian Psychiatric Association Journal,* 15:15–20, 1970.

Aserinsky, E., and Kleitman, N. Regularly occurring periods of eye motility and concomitant phenomena during sleep. *Science,* 118(3062):273–274, 1953.

Aserinsky, E., and Kleitman, N. Two types of ocular motility occurring in sleep. *Journal of Applied Physiology,* 8(1):1–10, 1955.

Ashby, W.R.; Collins, G.H.; and Bassett, M. The effects of nicotinic acid, nicotinamide, and placebo on the chronic schizophrenic. *The Journal of Mental Science,* 106(445):1555–1559, 1960.

Ashcroft, G.W.; Crawford, T.B.B.; Eccleston, D.; Sharman, D.F.; MacDougall, E.J.; Stanton, J.B.; and Binns, J.K. 5-Hydroxyindole compounds in the cerebrospinal fluid of patients with psychiatric or neurological diseases. *The Lancet,* II(7472):1049–1052, 1966.

Axelrod, J. Enzymatic formation of psychotomimetic metabolites from normally occurring compounds. *Science,* 134(3475):343, 1961.

Azumi, K. A polygraphic study of sleep in schizophrenics. *Seishin Shinkeigaku Zasshi,* 68:1222–1241, 1966.

Azumi, K.; Takahashi, S.; Takahashi, K.; Maruyama, N.; and Kikuti, S. The effects of dream deprivation on chronic schizophrenics and normal adults: A comparative study. *Folia Psychiatric et Neurologica Japonica,* 21:205–225, 1967.

Baldessarini, R.J. Factors influencing S-adenosyl methionine levels in mammalian tissues. In: Himwich, H.E.; Kety, S.S.; and Smythies, J.R., eds. *Amines and Schizophrenia.* Oxford: Pergamon Press, Inc., 1967. pp. 199–207.

Ban, T.A., and Lehmann, H.E. Nicotinic acid in the treatment of schizophrenia. *Canadian Psychiatric Association Journal,* 15:499–500, 1970.

Banerjee, S., and Agarwal, P.S. Tryptophan-nicotinic acid metabolism in schizophrenia. *Proceedings of the Society for Experimental Biology and Medicine,* 97(3):657–659, 1958.

Barbeau, A. Some biochemical disorders in Parkinson's disease—A review. *Journal of Neurosurgery,* 24:162–164, 1966.

Barbeau, A.; De Groot, J.A.; Joly, J.G.: Raymond-

Tremblay, D.; and Donaldson, J. Urinary excretion of a 3,4-dimethoxyphenylethylamine-like substance in Parkinson's disease. *Révue Canadiènne de Biologie,* 22(3–4): 469–472, 1963.

Beckett, P.G.S.; Senf, R.; Frohman, C.E.; and Gottlieb, J.S. Energy production and premorbid history in schizophrenia. *Archives of General Psychiatry,* 8(2):155–162, 1963.

Bell, C.E., and Somerville, A.R. Identity of the "pink spot." *Nature,* 211(5056):1405–1406, 1966.

Belton, N.R.; Backus, R.E.; and Millichap, J.G. Serum creatine phosphokinase activity in epilepsy. *Neurology,* 17(11):1073–1076, 1967.

Bengzon, A.; Hippius, H.; and Kanig, K. Some changes in the serum during treatment with psychotropic drugs. *The Journal of Nervous and Mental Disease,* 143(4):369–376, 1966.

Bergen, J.R. Biologic concomitants of schizophrenia. *Mental Hygiene,* 50(4):505–509, 1966.

Bergen, J.R. Plasma factors, amines and their derivatives in schizophrenia. *Research Communications in Chemical Pathology and Pharmacology,* 1(3):403–418, 1970.

Bergen, J.R.; Czicman, J.S.; and Koella, W.P. Influence of a plasma protein fraction from schizophrenic and normal persons upon the optic evoked response in the rabbit. *Journal of Neuropsychiatry,* 4(4):219–223, 1963.

Bergen, J.R.; Gray, F.W.; Pennell, R.B.; Freeman, H.; and Hoagland, H. Taraxein-like extracts: Effects on rat behavior. *Archives of General Psychiatry,* 12(1):80–82, 1965.

Bergen, J.R.; Mittag, T.W.; Frohman, C.E.; Arthur, R.E.; Warner, K.A.; Grinspoon, L.; and Freeman, H. Plasma factors in schizophrenia: Cooperative study. *Archives of General Psychiatry,* 18(4):471–476, 1968.

Berlet, H.H.; Matsumoto, K.; Pscheidt, G.R.; Spalde, J.; Bull, C.; and Himwich, H.E. Biochemical correlates of behavior in schizophrenic patients: Schizophrenic patients receiving tryptophan and methionine or methionine together with a monoamine oxidase inhibitor. *Archives of General Psychiatry,* 13(6):521–531, 1965.

Bernstein, J.; Mazur, W.P.; and Walaszek, E.J. The histaminolytic activity of serum from schizophrenic patients. *Medicina Experimentalis,* 2(5):239–244,1960.

Bishop, M.P. Effect of schizophrenic plasma upon original learning in the rat. *Diseases of the Nervous System,* 21(3):133–141, 1960.

Bishop, M.P.; Hollister, L.E.; Gallant, D.M.; and Heath, R.G. Ultracentrifugal serum proteins in schizophrenia. *Archives of General Psychiatry,* 15(4):337–340, 1966.

Bjurö, T.; Westling, H.; and Wetterqvist, H. On the evaluation of histamine formation and catabolism in rats by analysis of the urine. *Archives Internationales de Pharmacodynamie et de Théraple,* 144(3–4):337–346, 1963.

Boulton, A.A., and Felton, C.A. The "pink spot" and schizophrenia. *Nature,* 211(5056):1404–1405, 1966.

Boulton, A.A.; Pollitt, R.J.; and Majer, J.R. Identity of a urinary "pink spot" in schizophrenia and Parkinson's disease. *Nature,* 215(5097):132–134, 1967.

Bourdillon, R.E.; Clarke, C.A.; Ridges, A.P.; Sheppard, P.M.; Harper, P.; and Leslie, S.A. "Pink spot" in the urine of schizophrenics. *Nature,* 208:453–455, 1965.

Bourdillon, R.E., and Ridges, A.P. 3,4-Dimethoxyphenylethylamine in schizophrenia? In: Himwich, H.E.; Kety, S.S.; and Smythies, J.R., eds. *Amines in Schizophrenia.* New York: Pergamon Press, Inc., 1967. pp. 43–49.

Bowers, M.B., Jr.; Heninger, G.R.; and Gerbode, F. Cerebrospinal fluid 5-hydroxyindoleacetic acid and homovanillic acid in psychiatric patients. *International Journal of Neuropharmacology,* 8(3):255–262, 1969.

Brown, D.D.; Silva, O.L.; and McDonald, P. A comparison of the urinary metabolites of L-histidine-C^{14} in schizophrenic and normal subjects. *Journal of Psychiatric Research,* 1(2):101–105, 1962.

Brown, D.D.; Tomchick, R.; and Axelrod, J. The distribution and properties of a histamine-methylating enzyme. *The Journal of Biological Chemistry,* 234(11):2948–2950, 1959.

Brown, F.C. Blood factors in schizophrenia. *Archives of General Psychiatry,* 10(4):409–413, 1964.

Brown, W.T.; McGeer, P.L.; and Moser, I. Lack of psychotomimetic effect of para-methoxyphenylethylamine and 3,4-dimethoxyphenylethylamine in man. *Canadian Psychiatric Association Journal,* 13(1):91–92, 1968.

Brune, G.G., and Himwich, H.E. Effects of methionine loading on the behavior of schizophrenic patients. *The Journal of Nervous and Mental Disease,* 134(5):447–450, 1962a.

Brune, G.G., and Himwich, H.E. Indole metabolites in schizophrenic patients: Urinary excretion. *Archives of General Psychiatry,* 6(4):324–328, 1962b.

Brune, G.G; Hohl, H.H.; and Himwich, H.E. Urinary excretion of bufotenin-like substance in psychotic patients. *Journal of Neuropsychiatry,* 5(1):14–

17, 1963.

Buhler, D.R., and Ihler, G.S. Effect of plasma from normal and schizophrenic subjects on the oxidation of labeled glucose by chicken erythrocytes. *Journal of Laboratory and Clinical Medicine,* 62(2):306–318, 1963.

Bumpus, F.M., and Page, I.H. Serotonin and its methylated derivatives in human urine. *The Journal of Biological Chemistry,* 212(1):111–116, 1955.

Buscaino, G.A., and Stefanachi, L. The metabolism indole substances in diseases of the nervous system: Chromatographic studies of the urine of schizophrenics and other nervous patients. *Acta Neurologica,* 12(6):1188–1201, 1957.

Caldwell, D.F. Differential levels of stage IV sleep in a group of clinically similar chronic schizophrenic patients. *Biological Psychiatry,* 1(2):131–141, 1969.

Caldwell, D.F., and Domino, E.F. Electroencephalographic and eye movement patterns during sleep in chronic schizophrenic patients. *Electroencephalography and Clinical Neurophysiology,* 22(5):414–420, 1967.

Carlson, L.A.; Levi, L.; and Orö, L. Plasma lipids and urinary excretion of catecholamines in man during experimentally induced emotional stress, and their modification by nicotinic acid. *The Journal of Clinical Investigation,* 47(8):1795–1805, 1968.

Carpenter, W.T. Serotonin and depression. In: Sjoerdsma, A., ed. *Serotonin Now: Clinical Implication of Inhibiting Its Synthesis with Parachlorophenylalanine.* (Combined Clinical Staff Conference at the National Institutes of Health) *Annals of Internal Medicine,* 73:607–629, 1970.

Cassell, W.A., and Fisher, S. Body-image boundaries and histamine flare reaction. *Psychosomatic Medicine,* 25(4):344–350, 1963.

Cassell, W.A.; Newton, G.; and Cho, M. Serum histamine concentrations in schizophrenic and nonschizophrenic patients. *Journal of Schizophrenia,* 1(1):65–73, 1967.

Celesia, G.G., and Barr, A.N. Psychosis and other psychiatric manifestations of levodopa therapy. *Archives of Neurology,* 23(3):193–200, 1970.

Charalampous, K.D., and Tansey, L.W. Metabolic fate of β-(3,4-dimethoxyphenyl)-ethylamine in man. *The Journal of Pharmacology and Experimental Therapeutics,* 155(2):318–329, 1967.

Chase, T.N.; Schnur, J.A.; and Gordon, E.K. Cerebrospinal fluid monoamine catabolites in drug-induced extrapyramidal disorders. *Neuropharmacology,* 9(3):265–268, 1970.

Christodoulou, G.N., and Papaevangelou, G.J. High-protein, high-carbohydrate diets, and electroshock treatment related to 5-hydroxyindoleacetic acid excretion in schizophrenics and normal controls. *American Journal of Psychiatry,* 123(6):738–742, 1966.

Closs, K.; Wad, N.; and Ose, E. The "pink spot" in schizophrenia. *Nature,* 214(5087):483, 1967.

Cott, A. Treatment of ambulant schizophrenics with vitamin B_3 and relative hypoglycemic diet. *Journal of Schizophrenia,* 1(3):189–196, 1967.

Cowen, M.A. Studies of the transcephalic d.c. circuit: The histamine wheal in normal and psychiatric patients. *Behavioral Neuropsychiatry,* 1(3): 15–20, 1969.

Cremata, V.Y., Jr., and Koe, B.K. Clinical-pharmacological evaluation of p-chlorophenylalanine: A new serotonin-depleting agent. *Clinical Pharmacology and Therapeutics,* 7(6):768–776, 1966.

Creveling, C.R., and Daly, J.W. Identification of 3,4-dimethoxyphenethylamine from schizophrenic urine by mass spectrometry. *Nature,* 216(5111):190–191, 1967.

Dastur, D.K.; Mann, J.D.; and Pollin, W. Hippuric acid excretion, coffee, and schizophrenia. *Archives of General Psychiatry,* 9(1):79–82, 1963.

De Jong, H.H. *Experimental Catatonia. A General Reaction Form of the Central Nervous System and Its Implications for Human Pathology.* Baltimore, Md.: The Williams and Wilkins Company, 1945. 225 pp.

Dement, W. Dream recall and eye movements during sleep in schizophrenics and normals. *The Journal of Nervous and Mental Disease,* 122(3): 263–269, 1955.

Dement, W. The effect of dream deprivation. *Science,* 131(3415):1705–1707, 1960.

Dement, W.C. Experimental dream studies. In: Masserman, J.H., ed. *Academy of Psychoanalysis: Science and Psychoanalysis.* Vol. 7. New York: Grune & Stratton, Inc., 1964. pp. 129–184.

Dement, W.C. Psychophysiology of sleep and dreams. In: Arieti, S., ed. *Handbook of Psychiatry.* Vol. 3. New York: Basic Books, Inc., 1966. pp. 290–332.

Dement, W., and Fisher, C. Experimental interference with the sleep cycle. *Canadian Psychiatric Association Journal,* 8(6):400–405, 1963.

Dement, W., and Kleitman, N. Cyclic variations in EEG during sleep and their relation to eye movements, body motility, and dreaming. *Electroencephalography and Clinical Neurophysiology,* 9(4):673–690, 1957.

Dement, W.; Zarcone, V.; Ferguson, J.; Cohen,

H.; Pivik, T.; and Barchas, J. Some parallel findings in schizophrenic patients and serotonin-depleted cats. In: Sankar, D.V. Siva, ed. *Schizophrenia: Current Concepts and Research.* Hicksville, N.Y.: PJD Publications Ltd., 1969. pp. 775–811.

Denson, R. Nicotinamide in the treatment of schizophrenia. *Diseases of the Nervous System,* 23(3):167–172, 1962.

Domino, E.F.; Caldwell, D.F.; Henke, J.; and Henke, R. The differential effects of plasma from two groups of clinically similar schizophrenic patients on learning behavior in rats. *Journal of Psychiatric Research,* 4(2):87–94, 1966.

Dubo, H.; Park, D.C.; Pennington, R.J.T.; Kalbag, R.M.; and Walton, J.N. Serum-creatine-kinase in cases of stroke, head injury, and meningitis. *The Lancet,* II(7519):743–748, 1967.

Eisen, A.A., and Sherwin, A.L. Serum creatine phosphokinase activity in cerebral infarction. *Neurology,* 18(3):263–268, 1968.

Ellerbrook, R.C., and Purdy, M.B. Capacity of stressed humans under mega dosages of nicotinic acid to synthesize methylated compounds. *Diseases of the Nervous System,* 31(3):196–197, 1970.

Ellman, G.L.; Jones, R.T.; and Rychert, R.C. Mauve spot and schizophrenia. *American Journal of Psychiatry,* 125(6):849–851, 1968.

Engel, W.K., and Meltzer, H. Histochemical abnormalities of skeletal muscle in patients with acute psychoses. *Science,* 168(3928):273–276, 1970.

Engleman, K.; Lovenberg, W.; and Sjoerdsma, A. Inhibition of serotonin synthesis by parachlorophenylalanine in patients with the carcinoid syndrome. *New England Journal of Medicine,* 277: 1103–1108, 1967.

Ermala, P., and Autio, L. On intradermal histamine tests in schizophrenia. *Acta Psychiatrica et Neurologica Scandinavica* Supplement, 60:136–144, 1951.

Ernst, A.M. Phenomena of the hypokinetic rigid type cause by *O*-methylation of dopamine in the *para*-position. *Nature,* 193(4811):178–179, 1962.

Fabing, H.D., and Hawkins, J.R. Intravenous bufotenine injection in the human being. *Science,* 123(3203):886–887, 1956.

Faurbye, A., and Pind, K. Investigation on the occurrence of the dopamine metabolite 3,4-dimethoxyphenylethylamine in the urine of schizophrenics. *Acta Psychiatrica Scandinavica,* 40(3):240–243, 1964.

Faurbye, A., and Pind, K. Failure to detect 3,4-dimethoxyphenylethylamine in the urine of psychotic children. *Acta Psychiatrica Scandinavica* Supplement, 191:136–148, 1966.

Faurbye, A., and Pind, K. The catechol amine metabolism in schizophrenia. In: Walaas, O., ed. *Molecular Basis of Some Aspects of Mental Activity: Proceedings.* Vol. 2. New York: Academic Press, Inc., 1967. pp. 221–223.

Faurbye, A. and Pind, K. Occurrence of bufotenin in the urine of schizophrenic patients and normal persons. *Nature,* 220(5166):489, 1968.

Feinberg, I. Sleep electroencephalographic and eye-movement patterns in patients with schizophrenia and with chronic brain syndrome. In: Kety, S.S.; Evarts, E.V.; and Williams, H.L., eds. *Sleep and Altered States of Consciousness.* Baltimore, Md.: The Williams & Wilkins Company, 1967. pp. 211–240.

Feinberg, I. Recent sleep research: Findings in schizophrenia and some possible implications for the mechanism of action of chlorpromazine and for the neurophysiology of delirium. In: Sankar, D.V. Siva, ed. *Schizophrenia: Current Concepts and Research.* Hicksville, N.Y.: PJD Publications Ltd., 1969. pp. 739–750.

Feinberg, I.; Braun, M.; Koresko, R.L.; and Gottlieb, F. Stage 4 sleep in schizophrenia. *Archives of General Psychiatry,* 21(3):262–266, 1969.

Feinberg, I.; Braun, M.; and Shulman, E. EEG sleep patterns in mental retardation. *Electroencephalography and Clinical Neurophysiology,* 27(2):128–141, 1969.

Feinberg, I., and Evarts, E.V. Some implications of sleep research for psychiatry. In: Zubin, J., and Shagass, C., eds. *Neurobiological Aspects of Psychopathology.* New York: Grune & Stratton, Inc., 1969. pp. 334–393.

Feinberg, I.; Koresko, R.L.; and Gottlieb, F. Further observations on electrophysiological sleep patterns in schizophrenia. *Comprehensive Psychiatry,* 6(1):21–24, 1965.

Feinberg, I.; Koresko, R.L.; Gottlieb, F.; and Wender, P.H. Sleep electroencephalographic and eye-movement patterns in schizophrenic patients. *Comprehensive Psychiatry,* 5(1):44–53, 1964.

Feinberg, I.; Koresko, R.L.; and Heller, N. EEG sleep patterns as a function of normal and pathological aging in man. *Journal of Psychiatric Research,* 5(2):107–144, 1967.

Feldstein, A.; Hoagland, H.; and Freeman, H. Blood and urinary serotonin and 5-hydroxyindole acetic acid levels in schizophrenic patients and normal subjects. *The Journal of Nervous and Mental Disease,* 129(1):62–68, 1959.

Feldstein, A.; Hoagland, H.; and Freeman, H. Radioactive serotonin in relation to schizophrenia.

Archives of General Psychiatry, 5(3):246–251, 1961.

Ferguson, D.C., and Fisher, A.E. Behavior disruption in Cebus monkeys as a function of injected substances. *Science,* 139(3561):1281–1282, 1963.

Fessel, W.J. Disturbed serum proteins in chronic psychosis: Serological, medical, and psychiatric correlations. *Archives of General Psychiatry,* 4(2):154–159, 1961.

Fessel, W.J. Autoimmunity and mental illness: A preliminary report. *Archives of General Psychiatry,* 6(4):320–323, 1962a.

Fessel, W.J. Blood proteins in functional psychoses: A review of the literature and unifying hypothesis. *Archives of General Psychiatry,* 6(2): 132–148, 1962b.

Fessel, W.J. Macroglobulin elevations in functional mental illness. *Nature,* 193(4819):1005, 1962c.

Fessel, W.J. The "antibrain" factors in psychiatric patients' sera: I. Further studies with a hemagglutination technique. *Archives of General Psychiatry,* 8(6):614–621, 1963.

Fessel, W.J., and Grunbaum, B.W. Electrophoretic and analytical ultracentrifuge studies in sera of psychotic patients: Elevation of gamma globulins and macroglobulins, and splitting of alpha^2 globulins. *Annals of Internal Medicine,* 54(6):1134–1145, 1961.

Fessel, W.J.; Hirata-Hibi, M.; and Shapiro, I.M. Genetic and stress factors affecting the abnormal lymphocyte in schizophrenia. *Journal of Psychiatric Research,* 3:275–283, 1965.

Fischer, E.; Fernández Lagravere, T.A.; Vázquez, A.J.; and Di Stefano, A.O. A bufotenin-like substance in the urine of schizophrenics. *The Journal of Nervous and Mental Disease,* 133(5):441–444, 1961.

Fischer, E., and Spatz, H. Determinations of bufotenine in the urine of schizophrenia. *International Journal of Neuropsychiatry,* 3:226–228, 1967.

Fischer, E., and Spatz, H. Studies on urinary elimination of bufotenine-like substances in schizophrenia. *Biological Psychiatry,* 2(3):235–240, 1970.

Fischman, D.A.; Meltzer, H.Y.; and Poppel, R.W. Disruption of myofibrils in the skeletal muscle of psychotic patients. *Archives of General Psychiatry,* 23:503–515, 1970.

Fish, M.S., and Horning, E.C. Studies on hallucinogenic snuffs. *The Journal of Nervous and Mental Disease,* 124(1):33–37, 1956.

Fisher, C., and Dement, W.C. Studies on the psychopathology of sleep and dreams. *American Journal of Psychiatry,* 119(12):1160–1168, 1963.

Fragoso Mendes, J.M., and Lopes do Rosario, J.A. Signification et importance de la sérotonine en psychiatrie (Quelques résultats). *L'Encéphale,* 48(6):501–509, 1959.

Freedman, D.X.; Redlich, F.C.; and Igersheimer, W.W. Psychosis and allergy: Experimental approach. *American Journal of Psychiatry,* 112(11): 873–877, 1956.

Friedhoff, A.J., and Furiya, K. 3,4-Dimethoxyphenylacetic acid in urine. *Nature,* 214(5093):1127–1128, 1967.

Friedhoff, A.J., and Van Winkle, E. Isolation and characterization of a compound from the urine of schizophrenics. *Nature,* 194(4831):897–898, 1962.

Friedhoff, A.J., and Van Winkle, E. Conversion of dopamine to 3,4-dimethoxyphenylacetic acid in schizophrenic patients. *Nature,* 199(4900):1271–1272, 1963.

Friedhoff, A.J., and Van Winkle, E. A biochemical approach to the study of schizophrenia. *American Journal of Psychiatry,* 121(11):1054–1055, 1965.

Friedman, S.B.; Cohen, J.; and Iker, H. Antibody response to cholera vaccine: Differences between depressed, schizophrenic, and normal subjects. *Archives of General Psychiatry,* 16(3):312–315, 1967.

Frohman, C.E.; Beckett, P.G.S.; Grisell, J.L.; Latham, L.K.; and Gottlieb, J.S. Biologic responsiveness to environmental stimuli in schizophrenia. *Comprehensive Psychiatry,* 7(6):494–500, 1966.

Frohman, C.E.; Czajkowski, N.P.; Luby, E.D.; Gottlieb, J.S.; and Senf, R. Further evidence of a plasma factor in schizophrenia. *A.M.A. Archives of General Psychiatry,* 2(3):263–267, 1960a.

Frohman, C.E.; Latham, L.K.; Beckett, P.G.S.; and Gottlieb, J.S. Evidence of a plasma factor in schizophrenia. *A.M.A. Archives of General Psychiatry,* 2(3):255–262, 1960b.

Frohman, C.E.; Latham, L.K.; Warner, K.A.; Brosius, C.O.; Beckett, P.G.S.; and Gottlieb, J.S. Motor activity in schizophrenia: Effect on plasma factor. *Archives of General Psychiatry,* 9(1):83–88, 1963.

Frohman, C.E.; Tourney, G.; Beckett, P.G.S.; Lees, H.; Latham, L.K.; and Gottlieb, J.S. Biochemical identification of schizophrenia. *Archives of General Psychiatry,* 4(4):404–412, 1961.

Gallant, D.M.; Bishop, M.P.; and Steele, C.A. DPN (NAD-oxidized form): A preliminary evaluation in chronic schizophrenic patients. *Current Therapeutic Research,* 8(11):542, 1966.

Gardner, E.L. Chemically-induced alterations in the effect of schizophrenic plasma on rat behavior. American Institutes for Research-CTA Series No. 6, April, 1968. pp. 25–31.

German, G.A. Effects of serum from schizophrenics on evoked cortical potentials in the rat. *British Journal of Psychiatry,* 109(462):616–623, 1963.

German, G.A.; Antebi, R.N.; Dear, E.M.A.; and McCance, C. A further study of the effects of serum from schizophrenics on evoked cortical potentials in the rat. *British Journal of Psychiatry,* 111(473): 345–347, 1965.

Gershon, S.; Shopsin, B.; Bergen, J.R.; and Pinckney, L. Reevaluation of heterophile hemolytic response in psychiatric patients. *Archives of General Psychiatry,* 19(5):611–615, 1968.

Ghent, L., and Freedman, A.M. Comparison of effects of normal and schizophrenic serum on motor performance in rats. *American Journal of Psychiatry,* 115(5):465–466, 1958.

Gottlieb, J.S.; Frohman, C.E.; and Beckett, P.G.S. A theory of neuronal malfunction in schizophrenia. *American Journal of Psychiatry,* 126(2):149–156, 1969.

Gottlieb, J.S.; Frohman, C.E.; and Harmison, C.R. The structure of a unique protein in schizophrenia. Paper presented at the 123d Annual Meeting of the American Psychiatric Association, San Francisco, May, 1970.

Gowdey, C.W., and Lovegrove, T.D. Lack of differential effect of plasma from schizophrenic patients and normal subjects on performance of conditioned responses in rats. *Canadian Psychiatric Association Journal,* 11(4):286–298, 1966.

Green, J.P. Histamine and the nervous system. *Federation Proceedings,* 23(5):1095–1102, 1964.

Gross, H., and Franzen, F. Zur Bestimmung körpereigener Amine in biologischen Substraten. Beitrag zur Bestimmung von Bufotenin in menschlichem Blut und Harn. *Biochemische Zeitschrift,* 340(4):403–412, 1964.

Gulevich, G.D.; Dement, W.C.; and Zarcone, V.P. All-night sleep recordings of chronic schizophrenics in remission. *Comprehensive Psychiatry,* 8(3):141–149, 1967.

Gustafsson, A., and Forshell, G.P. Purification of a N-methyl-transferase. *Acta Chemica Scandinavica,* 17(2):541–542, 1963.

Haydu, G.G.; Dhrymiotis, A.; Korenyi, C.; and Goldschmidt, L. Effects of methionine and hydroxychloroquine in schizophrenia. *American Journal of Psychiatry,* 122(5):560–564, 1965.

Heath, R.G. Schizophrenia: Biochemical and physiologic aberrations. *International Journal of Neuropsychiatry,* 2:597–610, 1966.

Heath, R.G.; Cohen, S.B.; Silva, F.; Leach, B.E.; and Cohen, M. Administration of taraxein in humans. *Diseases of the Nervous System,* 20(5):206–208, 1959.

Heath, R.G., and the Department of Psychiatry and Neurology, Tulane University. *Studies in Schizophrenia.* Cambridge, Mass.: Harvard University Press, 1954. 610 pp.

Heath, R.G.; Guschwan, A.F.; and Coffey, J.W. Relation of taraxein to schizophrenia. *Diseases of the Nervous System,* 31(6):391–395, 1970.

Heath, R.G., and Krupp, I.M. Schizophrenia as an immunologic disorder: I. Demonstration of antibrain globulins by fluorescent antibody techniques. *Archives of General Psychiatry,* 16(1):1–9, 1967a.

Heath, R.G., and Krupp, I.M. The biologic basis of schizophrenia: An autoimmune concept. In: Walaas, O., ed. *Molecular Basis of Some Aspects of Mental Activity: Proceedings.* Vol. 2. New York: Academic Press, Inc., 1967b. pp. 313–344.

Heath, R.G., and Krupp, I.M. Schizophrenia as a specific biologic disease. *American Journal of Psychiatry,* 124(8):1019–1027, 1968.

Heath, R.G.; Krupp, I.M.; Byers, L.W.; and Liljekvist, J.I. Schizophrenia as an immunologic disorder: II. Effects of serum protein fractions on brain function. *Archives of General Psychiatry,* 16(1):10–23, 1967a.

Heath, R.G.; Krupp, I.M.; Byers, L.W.; and Liljekvist, J.I. Schizophrenia as an immunologic disorder: III. Effects of antimonkey and antihuman brain antibody on brain function. *Archives of General Psychiatry,* 16(1):24–33, 1967b.

Heath, R.G., and Leach, B.E. Brain recordings with schizophrenic behavior: Some metabolic factors responsible for physiological alterations. *Annals of the New York Academy of Sciences,* 96(1): 425–437, 1962.

Heath, R.G.; Martens, S.; Leach, B.E.; Cohen, M.; and Angel, C. Effect on behavior in humans with the administration of taraxein. *American Journal of Psychiatry,* 114(1):14–24, 1957.

Heller, B. Influence of treatment with an amino oxidase inhibitor on the excretion of bufotenin and the clinical symptoms in chronic schizophrenic patients. *International Journal of Neuropsychiatry,* 2:193–203, 1966.

Herjanic, M.; Moss-Herjanic, B.L.; and Paul, W.K. Treatment of schizophrenia with nicotinic acid. *Journal of Schizophrenia,* 1(3):197–199, 1967.

Heslinga, F.J.M.; Van Tilburg, W.; and Stam, F.C. The identity of the so-called pink spot in schizophrenia and Parkinson's disease. *Psychiatria, Neurologia, Neurochirurgia,* 73(3):157–164, 1970.

Hoagland, H. Biochemical aspects of schizophrenia. *The Journal of Nervous and Mental Disease,* 126(3):211–220, 1958.

Hoffer, A. *Niacin Therapy in Psychiatry.* Spring-

field, Ill.: Charles C Thomas, Publisher, 1962.

Hoffer, A. Nicotinic acid: An adjunct in the treatment of schizophrenia. *American Journal of Psychiatry,* 120(2):171–173, 1963.

Hoffer, A. The effect of nicotinic acid on the frequency and duration of re-hospitalization of schizophrenic patients; a controlled comparison study. *International Journal of Neuropsychiatry,* 2:234–240, 1966.

Hoffer, A., and Mahon, M. The presence of unidentified substances in the urine of psychiatric patients. *Journal of Neuropsychiatry,* 2(6):331–362, 1961.

Hoffer, A., and Osmond, H. Some schizophrenic recoveries. *Diseases of the Nervous System,* 23(4): 204–210, 1962.

Hoffer, A., and Osmond, H. Malvaria: A new psychiatric disease. *Acta Psychiatrica Scandinavica,* 39(2):335–366, 1963.

Hoffer, A., and Osmond, H. Treatment of schizophrenia with nicotinic acid: A 10 year follow-up. *Acta Psychiatrica Scandinavica,* 40(2):171–189, 1964.

Hoffer, A., and Osmond, H. Nicotinamide adenine dinucleotide (NAD) as a treatment for schizophrenia. *Journal of Psychopharmacology,* 1(3):79–95, 1966.

Hoffer, A., and Osmond, H. Nicotinamide adenine dinucleotide in the treatment of chronic schizophrenic patients. *British Journal of Psychiatry,* 114(512):915–917, 1968.

Hoffer, A.; Osmond, H.; Callbeck, M.J.; and Kahan, I. Treatment of schizophrenia with nicotinic acid and nicotinamide. *Journal of Clinical and Experimental Psychopathology,* 18(2):131–158, 1957.

Hollister, L.E., and Friedhoff, A.J. Effects of 3,4-dimethoxyphenylethylamine in man. *Nature,* 210 (5043):1377–1378, 1966.

Holmstedt, B. Gas chromatographic analysis of some psychoactive indole bases. In: Himwich, H.E.; Kety, S.S.; and Smythies, J.R., eds. *Amines and Schizophrenia.* New York: Pergamon Press, Inc., 1967. pp. 151–166.

Irvine, D.G. Apparently non-indolic Ehrlich-positive substances related to mental illnesses. *Journal of Neuropsychiatry,* 2(6):292–305, 1961.

Irvine, D.G.; Bayne, W.; Miyashita, H.; and Majer, J.R. Identification of kryptopyrrole in human urine and its relation to psychosis. *Nature,* 224(5221): 811–813, 1969.

Jodrey, L.H., and Smith, J.A. Releasable histamine levels and histamine tolerance in tissues of 291 psychotic patients. *American Journal of Psychiatry,* 115(9):801–807, 1959.

Jones, R.L.; Bory, P.; Brown, W.T.; and McGeer, P.L. Failure to detect p-methoxyphenylethylamine derivatives in human urine. *Canadian Journal of Biochemistry,* 47:185–195, 1969.

Jus, A.; Laskowska, D.; and Zimmy, S. Recherches sur le comportement, de la serotonine dans le seruon sanguin des schizophrènes. *Annales Médico-Psychologiques,* 116:898–912, 1958.

Kales, A.; Hoedemaker, F.S.; Jacobson, A.; and Lichtenstein, E.L. Dream deprivation: An experimental reappraisal. *Nature,* 204(4965):1337–1338, 1964.

Kety, S.S. Biochemical theories of schizophrenia. Part I. *Science,* 129(3362):1528–1532, 1959a.

Kety, S.S. Biochemical theories of schizophrenia. Part II. *Science,* 129(3363):1590–1596, 1959b.

Klee, G.D.; Bertino, J.; Goodman, A.; and Aronson, H. The effects of 5-hydroxytryptophan (a serotonin precursor) in schizophrenic patients. *The Journal of Mental Science,* 106(442):309–316, 1961.

Kline, N.S.; Barclay, G.L.; Cole, J.O.; Esser, A.H.; Lehmann, H.; and Wittenborn, J.R. Controlled evaluation of nicotinamide adenine dinucleotide in the treatment of chronic schizophrenic patients. *The British Journal of Psychiatry,* 113(500):731–742, 1967.

Kobayashi, Y., and Freeman, H. Histamine metabolism by schizophrenic and normal subjects. *Journal of Neuropsychiatry,* 3(2):112–117, 1961.

Kolyaskina, G.; Kushner, S.; and Gaskin, L. Certain immunological changes in schizophrenic patients. In: Snezhnevsky, A., ed. *Biological Research in Schizophrenia.* Moscow: Academy of Medical Sciences of the U.S.S.R., Institute of Psychiatry, 1967. pp. 238–240.

Kopin, I.J. Tryptophan loading and excretion of 5-hydroxyindoleacetic acid in normal and schizophrenic subjects. *Science,* 129(3352):835–836, 1959.

Koresko, R.L.; Snyder, F.; and Feinberg, I. "Dream time" in hallucinating and non-hallucinating schizophrenic patients. *Nature,* 199(4898):1118–1119, 1963.

Krasnova, A. The effect of the serum of relatives of schizophrenic patients on the lactate-pyruvate ratio in vitro experiments. In: Snezhnevsky, A., ed. *Biological Research in Schizophrenia.* Moscow: Academy of Medical Sciences of the U.S.S.R., Institute of Psychiatry, 1967. pp. 262–263.

Kuehl, F.A., Jr.; Hichens, M.; Ormond, R.E.; Meisinger, M.A.P.; Gale, P.H.; Cirillo, V.J.; and Brink, N.G. *Para-O*-methylation of dopamine in schizophrenic and normal individuals. *Nature,* 203(4941):

154–155, 1964.

Kuehl, F.A., Jr.; Ormond, R.E.; and Vandenheuvel, W.J.A. Occurrence of 3,4-dimethoxyphenylacetic acid in urines of normal and schizophrenic individuals. *Nature,* 211(5049):606–608, 1966.

Kunugi, H. All-night sleep EEG in chronic schizophrenia. *Seishin Shinkeigaku Zasshi,* 72:202–226, 1970.

Kupfer, D.J.; Wyatt, R.J.; Scott, J.; and Snyder F. Sleep disturbance in acute schizophrenic patients. *American Journal of Psychiatry,* 126:1213–1223, 1970.

Kuznetsova, N. Some data concerning the immunological properties of brain mitochondria. In: Snezhnevsky, A., ed. *Biological Research in Schizophrenia.* Moscow: Academy of Medical Sciences of the U.S.S.R., Institute of Psychiatry, 1967. pp. 221–223.

Lalry, G.C. Donnes recentes sur la physiologie et la phyciopathologie de l'activite onirique. In: Lopez-Ibor, J.J., ed. *Excerpta Medica.* Madrid, Spain: Congress Series No. 150, 1:189–196, 1966.

Lalry, G.C.; Barte, H.; Golsteinas, L.; and Ridjanovic, S. Sommell de nuit des malades mentaus. In: *Le Sommell et Nuit Normal et Pathologique Etudes Electroencéphalographiques.* Paris: Masson and Cie, Nouvelle Serie 2, 1965. pp. 354–381.

Lang, R.W., and Corvin, A. Rabbit erythrocyte hemagglutinins in schizophrenia. *Archives of General Psychiatry,* 21(6):665–672, 1969.

Lauer, J.W.; Inskip, W.M.; Bernsohn, J.; and Zeller, E.A. Observations on schizophrenic patients after iproniazid and tryptophan. *A.M.A. Archives of Neurology and Psychiatry,* 80(1):122–130, 1958.

Leblanc, J., and Lemieux, L. Histamine and mental disease. *Medicina Experimentalis,* 4(4):214–222, 1961.

Lester, B.K.; Burch, N.R.; and Dossett, R.C. Nocturnal EEG–GSR profiles: The influence of presleep states. *Psychophysiology,* 3:238–248, 1967.

Leyton, G.B. Indolic compounds in the urine of schizophrenics. *British Medical Journal,* 2(5105): 1136–1339, 1958.

Lideman, R., and Bokova, I. The possible nature and mechanism of the action of the active factor of the blood serum of schizophrenic patients. In: Snezhnevsky, A., ed. *Biological Research in Schizophrenia.* Moscow: Academy of Medical Sciences of the U.S.S.R., Institute of Psychiatry, 1967. pp. 169–171.

Ljungberg, E. 5-Hydroxyindole-3-acetic acid excretion in the urine, a specific diagnostic sign in fatal catatonia. *West European Symposia on Clinical Chemistry,* 2:169–170, 1963.

Logan, D.G., and Deodhar, S.D. Schizophrenia, an immunologic disorder? *Journal of the American Medical Association,* 212(10):1703–1704, 1970.

Lovett Doust, J.W.; Husdan, H.; and Salna, M.E. Blood-histamine and tissue-cell anoxia in mental disease. *Nature,* 178(4531):492, 1956.

Lovegrove, T.D., and Nicholls, D.M. Haptoglobin subtypes in a schizophrenic and control population. *The Journal of Nervous and Mental Disease,* 141(2): 195–196, 1965.

Lozovsky, D.; Krasnova, A.; Factor, M.; Polyanskaya, N.; and Popova, N. The effect of the serum of schizophrenic patients upon certain glucose transformation indices in experiment. In Snezhnevsky, A., ed. *Biological Research in Schizophrenia.* Moscow: Academy of Medical Sciences of the U.S.S.R., Institute of Psychiatry, 1967. pp. 151–155.

Lucy, J.D. Histamine tolerance in schizophrenia. *A.M.A. Archives of Neurology and Psychiatry,* 71(5): 629–639, 1954.

Mandell, A.J., and Morgan, M. Human brain enzyme makes indole hallucinogens. (Abstract) *Proceedings of the 1970 American Psychological Association Meeting.* p. 228.

Mandell, A.J., and Younger, C.B. Asthma alternating with psychiatric symptomatology. *California Medicine,* 96(4):251–253, 1962.

Mangoni, A.; Balazs, R.; and Coppen, A.J. The effect of plasma from schizophrenic patients on the chicken erythrocyte system. *British Journal of Psychiatry,* 109(459):231–234, 1963.

Mann, J.D., and LaBrosse, E.H. Urinary excretion of phenolic acids by normal and schizophrenic male patients. *A.M.A. Archives of General Psychiatry,* 1(5):547–551, 1959.

Marshall, P.B. Effect of sex hormones on the excretion of free histamine by male and female rats. *British Journal of Pharmacology and Chemotherapy,* 16(1):50–58, 1961.

Masur, J.; Breda, J.B.; Bueno, O.F.A.; and Carlini, E.A. Failure of plasma from schizophrenics to potentiate the effects of 3,4-dimethoxyphenylethylamine on rats and mice. *Archives Internationales de Pharmacodynamie et de Thérapie,* 179(1):56–64, 1969.

Melander, B., and Martens, S. The mode of action of taraxein and LSD. *Diseases of the Nervous System,* 19(11):478–479, 1958.

Meltzer, H. Creatine kinase and aldolase in serum: Abnormality common to acute psychoses. *Science,* 159(3821):1368–1370, 1968.

Meltzer, H. Muscle enzyme release in the acute

psychoses. *Archives of General Psychiatry,* 21(7): 102–112, 1969a.

Meltzer, H. Reply to Warnock and Ellman. *Science,* 164(3880):726–727, 1969b.

Meltzer, H. Increased activity of creatine phosphokinase and aldolase activity in the acute psychoses: Case reports. *Journal of Psychiatric Research,* 7(4): 249–262, 1970.

Meltzer, H.Y., and Boyer, M. Effect of blood serum or plasma from schizophrenic patients and others on an action of 3,4-dimethoxyphenylethylamine: A failure to replicate. *Archives Internationales de Pharmacodynamie et de Thérapie,* 182 (2):481–488, 1969.

Meltzer, H.; Elkun, L.; and Moline, R.A. Serum-enzyme changes in newly admitted psychiatric patients. Part I. *Archives of General Psychiatry,* 21(6):731–738, 1969.

Meltzer, H.Y., and Engel, W.K. Histochemical abnormalities of skeletal muscle in acutely psychotic patients. *Archives of General Psychiatry,* 23: 492–502, 1970.

Meltzer, H.Y.; Kupfer, D.J.; Wyatt, R.; and Snyder, F. Sleep disturbance and serum CPK activity in acute psychosis. *Archives of General Psychiatry,* 22(5):398–405, 1970a.

Meltzer, H.Y., and Moline, R. Muscle abnormalities in acute psychosis. *Archives of General Psychiatry,* 23:481–491, 1970b.

Meltzer, H.Y., and Moline, R. Plasma enzymatic activity after exercise: Study of psychiatric patients and their relatives. *Archives of General Psychiatry,* 22(5):390–397, 1970a.

Meltzer, H.; Pahnke, W.; Kurland, A.; and Henkin, R. Serum CPK and aldolase activity in man following controlled administration of psychotomimetic drugs. *Psychopharmacologia,* 16(5):419–425, 1970b.

Meltzer, H.; Shader, R.; and Grinspoon, L. The behavioral effects of nicotinamide adenine dinucleotide in chronic schizophrenia. *Psychopharmacologia,* 15(2):144–152, 1969.

Mendels, J., and Hawkins, D.R. Sleep studies in depression. Paper presented at NIMH seminar on "Recent Advances in the Psychobiology of the Depressive Illness," Williamsburg, Virginia, 1969, in press.

Mosher, L.R. Nicotinic acid side effects and toxicity: A review. *American Journal of Psychiatry,* 126(9):1290–1296, 1970.

Mosher, L.R., and Feinsilver, D. *Special Report on Schizophrenia.* U.S. Department of Health, Education, and Welfare, Public Health Service, Health Services and Mental Health Administration, National Institute of Mental Health, April, 1970.

Narasimhachari, N.; Heller, B.; Spaide, J.; Haskovec, L.; Fujimori, M.; Tabushi, K.; and Himwich, H.E. Comparative behavioral and biochemical effects of tranylcypromine and cysteine on normal controls and schizophrenic patients. *Life Sciences,* 9(1):1021–1032, 1970.

Nichols, R.E.; Sugerman, A.A.; and Murphree, H.B. Effects of nicotinamide adenine dinucleotide (NAD) and its precursors on whole blood NAD levels and on the quantitative electroencephalogram (EEG). (Abstract) *Federation Proceedings,* 26(2):505, 1967.

Nishimura, T., and Gjessing, L.R. Failure to detect 3,4-dimethoxyphenylethylamine and bufotenine in the urine from a case of periodic catatonia. *Nature,* 206(4987):963–964, 1965.

Nunn, R.F., and Wheeler, R.H. Is brain damage the cause of "pink spot"? *Nature,* 212(5065):939, 1966.

O'Reilly, P.O.; Ernest, M.; and Hughes, G. The incidence of malaria. *The British Journal of Psychiatry,* 111:741–744, 1965.

O'Reilly, P.O.; Hughes, G.; Russell, S.; and Ernest, M. The mauve factor: An evaluation. *Diseases of the Nervous System,* 26(9):562–568, 1965.

Ornitz, E.M.; Ritvo, E.R.; Panman, L.M.; Lee, Y.H.; Carr, E.M.; and Walter, R.D. The auditory evoked response in normal and autistic children during sleep. *Electroencephalography and Clinical Neurophysiology,* 25(3):221–230, 1968.

Osmond, H., and Hoffer, A. Massive niacin treatment in schizophrenia: Review of a nine-year study. *The Lancet,* I(7224):316–319, 1962.

Osmond, H., and Smythies, J. Schizophrenia: A new approach. *The Journal of Mental Science,* 98 (411):309–315, 1952.

Park, L.C.; Baldessarini, R.J.; and Kety, S.S. Methionine effects on chronic schizophrenics: Patients treated with monoamine oxidase inhibitors. *Archives of General Psychiatry,* 12(4):346–351, 1965.

Pauling, L. Orthomolecular psychiatry. *Science,* 160(3825):265–271, 1968.

Pennell, R.B.; Pawlus, C.; Saravis, C.A.; and Scrimshaw, G. Chemical characteristics of a plasma fraction which influences animal behavior. In: Walaas, O., ed. *Molecular Basis of Some Aspects of Mental Activity: Proceedings.* Vol. 2. New York: Academic Press, Inc., 1967. pp. 269–282.

Perry, T.L. N-methylmetanephrine: Excretion by juvenile psychotics. *Science,* 139(3555):587–589, 1963.

Perry, T.L.; Hansen, S.; and MacDougall, L. Identity and significance of some pink spots in schizophrenia and other conditions. *Nature,* 214 (5087):484–485, 1967.

Perry, T.L.; Hansen, S.; MacDougall, L.; and Schwarz, C.J. Urinary amines in chronic schizophrenia. *Nature,* 212(5058):146–148, 1966.

Perry, T.L.; Hansen, S.; and Macintyre, L. Failure to detect 3,4-dimethoxyphenylethylamine in the urine of schizophrenics. *Nature,* 202(4931):519–520, 1964.

Perry, T.L.; Shaw, K.N.F.; Walker, D.; and Redlich, D. Urinary excretion of amines in normal children. *Pediatrics,* 30(4):576–584, 1962.

Persson, T., and Roos, B.E. Acid metabolites from monoamines in cerebrospinal fluid of chronic schizophrenics. *British Journal of Psychiatry,* 115 (518):95–98, 1969.

Pfeiffer, C.C.; Iliev, V.; Jenney, E.H.; and Cawley, J. Histamine polyamines and trace metals in the schizophrenias. Paper presented at the International Congress of Neuropharmacology, 1970.

Pind, K., and Faurbye, A. Does 3,4-dimethoxyphenylethylamine occur in the urine from schizophrenics and normal persons? *Acta Psychiatrica Scandinavica,* 42(3):246–251, 1966.

Pivik, T., and Dement, W.C. Phasic changes in muscular and reflex activity during non-REM sleep. *Experimental Neurology,* 27(1):115–124, 1970.

Pollin, W.; Cardon, P.V., Jr.; and Kety, S.S. Effects of amino acid feedings in schizophrenic patients treated with iproniazid. *Science,* 133(3446): 104–105, 1961.

Predescu, V.; Florescu, D.; and Radulescu, C. Pink spot as a diagnostic test in schizophrenia. *Nature,* 217(5134):1150–1151, 1968.

Proctor, C.D.; Cho, J.B.; Potts, J.L.; Ashley, L.G.; Douglas, J.G.; Amoroso, C.P.; McGriff, J.E.; and Eaton, H.E., Jr. An influence of blood plasma from schizophrenics on an action of 3,4-dimethoxyphenylethylamine. *Archives Internationales de Pharmacodynamie et de Thérapie,* 172(1):95–105, 1968.

Pue, A.F.; Hoare, R.; and Adamson, J.D. The "pink spot" and schizophrenia. *Canadian Psychiatric Association Journal,* 14:397–401, 1969.

Rechtschaffen, A.; Molinari, S.; Watson, R.; and Wincor, M. "Extracular Potentials: A Possible Indicator of PGO Activity in the Human." Paper presented at Association for Psychophysiological Study of Sleep, Santa Fe, N.M., 1970.

Rechtschaffen, A.; Schulsinger, F.; and Mednick, S.A. Schizophrenia and physiological indices of dreaming. *Archives of General Psychiatry,* 10(1): 89–93, 1964.

Ridges, A.P., and Harper, P. Pink spot—Is it a drug artifact? *Psychiatria Clinica,* 3(2):101–107, 1970.

Rinne, U.K., and Sonninen, V. Urinary excretion of 3,4-dimethoxyphenylethylamine in Parkinson's disease. *Nature,* 216(5114):489, 1967.

Robins, E. Discussion of paper by R.G. Heath. In: Abramson, H.A., ed. *Neuropharmacology.* New York: Josiah Macy, Jr., Foundation, 1957. p. 123.

Rodnight, R. Body fluid indoles in mental illness. *International Review of Neurobiology,* 3:251–292, 1961.

Rosengarten, H.; Piotrowski, A.; Romaszewska, K.; Szemis, A.; Jus, A.; and Matsumoto, H. The occurrence of N,N-dimethyltryptamine and bufotenine in schizophrenic patients without MAO blockage and methionine loading. Paper presented at the International Congress of Neuropharmacology, 1970.

Rubin, R.T. Investigation of precipitins to human brain in sera of psychotic patients. *British Journal of Psychiatry,* 111(479):1003–1006, 1965.

Runge, T.M.; Lara, F.Y.; Thurman, M.T.; Keyes, J.W.; and Hoerster, S.H., Jr. Search for a bufotenin-like substance in the urine of schizophrenics. *The Journal of Nervous and Mental Disease, 142* (5):470–474, 1966.

Ryan, J.W.; Steinberg, H.R.; Green, R.; Brown, J.D.; and Durell, J. Controlled study of effects of plasma of schizophrenic and non-schizophrenic psychiatric patients on chicken erythrocytes. *Journal of Psychiatric Research,* 6(1):33–43, 1968.

Sampson, H. Psychological effects of deprivation of dreaming sleep. *The Journal of Nervous and Mental Disease,* 143(4):305–317, 1966.

Sanders, B.E.; Small, S.M.; Ayers, W.J.; Oh, Y.H.; and Axelrod, S. Additional studies on plasma proteins obtained from schizophrenics and controls. *Transactions of the New York Academy of Sciences,* 28(1):22–39, 1965.

Sanders, E., and Bush, M.T. Distribution, metabolism and excretion of bufotenine in the rat with preliminary studies of its O-methyl derivative. *The Journal of Pharmacology and Experimental Therapeutics,* 158(2):340–352, 1967.

Schiavone, D.J., and Kaldor, J. Creatine phosphokinase levels and cerebral disease. *The Medical Journal of Australia,* II(19):790–792, 1965.

Seal, U.S., and Eist, H. Elevation of serum protein-bound carbohydrates and haptoglobin in schizophrenia. *Clinical Chemistry,* 12(10):709–716, 1966.

Seal, U.S., and Swaim, W.R. Plasminogen levels in schizophrenia. *Clinical Chemistry,* 14(4):368–370, 1968.

Seal, U.S.; Swaim, W.R.; and Eist, H. Hyper-

fibrinogenemia in schizophrenia. *Clinical Chemistry,* 13:160–162, 1967.

Semenov, S.; Glevov, V.; and Chuprikov, A. Autoimmune organispecific reactions as one of the factors of pathobiology of schizophrenia. In: Snezhnevsky, A., ed. *Biological Research in Schizophrenia.* Moscow: Academy of Medical Sciences of the U.S.S.R. Institute of Psychiatry, 1967. pp. 230–233.

Sen, N.P., and McGeer, P.L. 4-Methoxyphenylethylamine and 3,4-dimethoxyphenylethylamine in human urine. *Biochemical and Biophysical Research Communications,* 14(3):227–232, 1964.

Shaw, C.R.; Lucas, J.; and Rabinovitch, R.D. Metabolic studies in childhood schizophrenia: Effects of tryptophan loading on indole excretion. *A.M.A. Archives of General Psychiatry,* 1(4):366–371, 1959.

Sherwood, S.L. The response of psychotic patients to intraventricular injections. *Proceedings of the Royal Society of Medicine,* 48(10):855–863, 1955.

Shulgin, A.T.; Sargent, T.; and Naranjo, C. Role of 3,4-dimethoxyphenethylamine in schizophrenia. *Nature,* 212(5070):1606–1607, 1966.

Siegel, M. A sensitive method for detection of n, n-dimethylserotonin (bufotenin) in urine; failure to demonstrate its presence in the urine of schizophrenic and normal subjects. *Journal of Psychiatric Research,* 3:205–211, 1965.

Siegel, M.; Niswander, G.D.; Sachs, E., Jr.; and Stavros, D. Taraxein, fact or artifact? *American Journal of Psychiatry,* 115(9):819–820, 1959.

Simpson, G.M., and Kline, N.S. Histamine wheal formation and mental illness. *The Journal of Nervous and Mental Disease,* 133(1):19–24, 1961.

Sireix, D.W., and Marini, F.A. Bufotenine in human urine. *Biological Psychiatry,* 1(2):189–191, 1969.

Smith, K.; Thompson, G.F.; and Koster, H.D. Sweat in schizophrenic patients: Identification of the odorous substance. *Science,* 166(3903):398–399, 1969.

Smythies, J.R. *Biological Psychiatry.* London: William Heinemann Medical Books Ltd., 1968.

Smythies, J.R., and Antun, F. The biochemistry of psychosis. *Scottish Medical Journal,* 15(1):34–40, 1970.

Smythies, J.R.; Benington, F.; and Morin, R.D. The biochemical lesion in schizophrenia. In: Sankar, D.V. Siva, ed. *Schizophrenia: Current Concepts and Research.* Hicksville, N.Y.: PJD Publications Ltd., 1969. pp. 486–495.

Smythies, J.R.; Benington, F.; and Morin, R.D. The mechanism of action of hallucinogenic drugs on a possible serotonin receptor in the brain. *International Review of Neurobiology,* 12:207–233, 1970.

Snyder, F. Disturbance of the EEG sleep patterns in relation to acute psychosis. In: Sankar, D.V. Siva, ed. *Schizophrenia: Current Concepts and Research.* Hicksville, N.Y.: PJD Publications Ltd., 1969. pp. 751–774.

Sohler, A.; Renz, R.H.; Smith, S.; and Kaufman, J. Significance of hydroxyskatole and mauve factor excretion in schizophrenia. *International Journal of Neuropsychiatry,* 3(4):327–331, 1967.

Sohler, A.; Beck, R.; and Novel, J.M. Mauve factor re-identified as 2,4-dimethyl-3-ethylpyrrole and its sedative effect on the CNS. *Nature,* 228:1318–1320, 1970.

Solomon, G.F.; Allansmith, M.; McClellan, B.; and Amkraut, A. Immunoglobulins in psychiatric patients. *Archives of General Psychiatry,* 20(3):272–277, 1969.

Spaide, J.; Neveln, L.; Tolentino, J.; and Himwich, H.E. Methionine and tryptophan loading in schizophrenic patients receiving a MAO inhibitor: Correlation of behavioral and biochemical changes. *Biological Psychiatry,* 1(3):227–233, 1969.

Spaide, J.; Tanimukai, H.; Bueno, J.R.; and Himwich, H.E. Behavioral and biochemical alterations in schizophrenic patients. *Archives of General Psychiatry,* 18(6):658-665, 1968.

Spaide, J.; Tanimukai, H.; Ginther, R.; Bueno, J.; and Himwich, H.E. Schizophrenic behavior and urinary tryptophan metabolites associated with cysteine given with and without a monoamine oxidase inhibitor (tranylcypromine). *Life Sciences,* 6(5):551–560, 1967.

Sprince, H.; Parker, C.M.; Jameson, D.; and Alexander, F. Urinary indoles in schizophrenic and psychoneurotic patients after administration of tranylcypromine (Parnate) and methionine or tryptophan. *The Journal of Nervous and Mental Disease,* 137(3):246–251, 1963.

Stabenau, J.R.; Creveling, C.R.; and Daly, J. Common tea as a source for 3,4-dimethoxyphenylethylamine, or "pink spot" in the urine of schizophrenics and normals. Paper presented at the International Congress of Neuropharmacology, 1970.

Stabenau, J.R.; Pollin, W.; Mosher, L.R.; Frohman, C.; Friedhoff, A.J.; and Turner, W. Study of monozygotic twins discordant for schizophrenia: Some biologic variables (lactate-pyruvic ratio; 3,4-dimethoxyphenlethylamine; S_{19} macroglobulin; antirabbit red cell hemagglutin; protein bound iodine). *Archives of General Psychiatry,* 20(2):145–158, 1969.

Stam, F.C.; Heslinga, F.J.M.; and Van Tilburg, W. Schizophrenia and pink spot. *Psychiatria, Neurologia, Neurochirurgia,* 72(6):513–524, 1969.

Stein, L., and Wise, C.D. Possible etiology of schizophrenia: Progressive damage to the noradrenergic reward system by 6-hydroxydopamine. *Science,* 171(3975): 1032–1036, 1971.

Steinberg, H.R., and Robinson, J. Nor$_2$chlorpromazine sulphoxide and 3,4-dimethoxyphenethylamine. *Nature,* 217(5133):1054–1055, 1968.

Stenhouse, D.; Antebi, R.; Dear, E.M.A.; Herrington, R.N.; and McCance, C. Effect of serum from schizophrenics on evoked cortical potentials in the rat. *British Journal of Psychiatry,* 111(473):339–344, 1965.

Stern, M.; Fram, D.H.; Wyatt, R.; Grinspoon, L.; and Tursky, B. All-night sleep studies of acute schizophrenics. *Archives of General Psychiatry,* 20(4):470–477, 1969.

Stern, P.; Hukovic, S.; Madjerek, Z.; and Karabaic, S. Histamingehalt im Blute von Schizophrenikern. *Archives Internationales de Pharmacodynamie et de Thérapie,* 109(3–4):294–299, 1957.

Stewart, C.N., and Irvine, D.G. Effect of blood plasma from schizophrenic patients upon avoidance conditioning in the rat. *Diseases of the Nervous System,* 23(8):456–460, 1962.

Strahilevitz, M., and Davis, S.D. Increased IgA in schizophrenic patients. *The Lancet,* II:370, 1970.

Strengers, T., and Gooszen, J.A.H. Le taux sanguin de l'histamine chez les schizophrènes. *L'Encéphale,* 36(10):283–287, 1946–1947.

Studnitz, W., and Nyman, G.E. Excretion of 3,4-dimethoxyphenylethylamine in schizophrenia. *Acta Psychiatrica Scandinavica,* 41(1):117–121, 1965.

Sullivan, T.M.; Frohman, C.E.; Beckett, P.G.S.; and Gottlieb, J.S. Biochemical studies of families of schizophrenic patients. *American Journal of Psychiatry,* 122(9):1040–1044, 1966.

Sullivan, T.M.; Frohman, C.E.; Beckett, P.G.S.; and Gottlieb, J.S. Clinical and biochemical studies of families of schizophrenic patients. *American Journal of Psychiatry,* 123(8):947–952, 1967.

Takesada, M.; Kakimoto, Y.; Sano, I.; and Kaneko, Z. 3,4-Dimethoxyphenylethylamine and other amines in the urine of schizophrenic patients. *Nature,* 199(4889):203–204, 1963.

Tanimukai, H.; Ginther, R.; Spaide, J.; Bueno, J.R.; and Himwich, H.E. Occurrence of bufotenin (5-hydroxy-N,N-dimethyltryptamine) in urine of schizophrenic patients. *Life Sciences,* 6:1697–1706, 1967a.

Tanimukai, H.; Ginther, R.; Spaide, J.; Bueno, J.R.; and Himwich, H.E. Psychotogenic N,N-dimethylated indole amines and behavior in schizophrenic patients. In: Wortis, J., ed. *Recent Advances in Biological Psychiatry.* Vol. X. New York: Plenum Press, 1968. pp. 6–15.

Tanimukai, H.; Ginther, R.; Spaide, J.; and Himwich, H.E. Psychotomimetic indole compound in the urine of schizophrenics and mentally defective patients. *Nature,* 216:490–491, 1967b.

Throne, M.L.; Gowdey, C.W.; and Lovegrove, T.D. Effect of plasma from chronic schizophrenic and normal subjects on the rate of acquisition of a conditioned avoidance response by rats. *Journal of Nervous and Mental Disease,* 142(3):248–253, 1966.

Tikhonov, V.; Lozovsky, D.; and Glezer, I. Effect of blood serum from schizophrenic patients upon potassium ion stimulated respiration of rat brain slices. In: Snezhnevsky, A., ed. *Biological Research in Schizophrenia.* Moscow: Academy of Medical Sciences of the U.S.S.R. Institute of Psychiatry, 1967. pp. 156–157.

Turner, W.J., and Chipps, H.I. A heterophile hemolysin in human blood. I. Distribution in schizophrenics and non schizophrenics. *Archives of General Psychiatry,* 15:373–377, 1966.

Turner, W.J., and Merlis, S. Effect of some indolealkylamines on man. *A.M.A. Archives of Neurology and Psychiatry,* 81(1):121–129, 1959.

Turner, W.J., and Turano, P.A. Anti-rabbit heterophile hemolysin and agglutinin in human serum: Failure to corroborate previous observations on schizophrenics. *Archives of General Psychiatry,* 19(5):616–618, 1968.

Uzunov, G.; Iordanov, B.; and Doseva, I. Cellular membrane permeability in schizophrenia. In: Snezhnevsky, A., ed. *Biological Research in Schizophrenia.* Moscow Academy of Medical Sciences of the U.S.S.R., Institute of Psychiatry, 1967. pp. 166-168.

Vincent, J.D.; Favarel-Garrigues, B.; Bourgeois, M.; and Dufy, B. [Night sleep of the schizophrenic at the start of evolution: Polygraphic study by telemetry.] Sommeil de nuit du schizophrène en début d'évolution: Étude polygraphique par télémesure. *Annales Médico-Psychologiques* (Paris), 2(2):227–235, 1968.

Vogel, G.W., and Traub, A.C. REM deprivation. I. The effect on schizophrenic patients. *Archives of General Psychiatry,* 18(3):287–300, 1968.

Vogel, W.H. Physiological disposition and metabolism of 3,4-dimethoxyphenylethylamine in the rat. *International Journal of Neuropharmacology,* 7(4):373–381, 1968.

Vogel W.H.; Ahlberg, C.D.; and Horwitt, M.K. Time study of urinary excretion of 3,4-dimethoxyphenylethylamine and 3,4 dimethoxyphenylacetic acid by schizophrenic and normal individuals. *International Journal of Neuropsychiatry,* 3:292–297, 1967.

Wagner, A.F.; Cirillo, V.J.; Meisinger, M.A.P.; Ormond, R.E.; Kuehl, F.A., Jr.; and Brink, N.G. A further study of catecholamine *O*-methylation in schizophrenia. *Nature,* 211(5049):604–605, 1966.

Warnock, D.G., and Ellman, G.L. Intramuscular chlorpromazine and creatine kinase: Acute psychoses or local muscle trauma? *Science,* 164(3880): 726, 1969.

Watt, J.A.G.; Ashcroft, G.W.; Daly, R.J.; and Smythies, J.R. Urine volume and pink spots in schizophrenia and health. *Nature,* 221(5184):971–972, 1969.

Weblin, J.E. Psychogenesis in asthma: An appraisal with a view to family research. *British Journal of Medical Psychology,* 36(3):211–225, 1963.

Weckowicz, T.E., and Hall, R. Skin histamine reaction in schizophrenic and non-schizophrenic mental patients. *The Journal of Nervous and Mental Disease,* 126(5):415–420, 1958.

Welch, J.P.; Clower, C.G.; and Schimke, R.N. The "pink spot" in schizophrenics and its absence in homocystinurics. *British Journal of Psychiatry,* 115 (519):163–167, 1969.

White, T.J. Inhibition of the methylation of histamine in cat brain. *British Journal of Physiology,* 159:191, 1961.

Whittingham, S.; Mackay, I.R.; Jones, I.H.; and Davies, B. Absence of brain antibodies in patients with schizophrenia. *British Medical Journal,* 1(5588): 347–348, 1968.

Widelitz, M.M., and Feldman, W. Pink spot in childhood schizophrenia. *Behavioral Neuropsychiatry,* 1(1):29–30, 1969.

Willlams, C.H.; Gibson, J.G.; and McCormick, W.O. 3,4-dimethoxyphenylethylamine in schizophrenia. *Nature,* 211(5054):1195, 1966.

Wilson, W.P., and Nashold, B.S. The sleep rhythms of subcortical nuclei: Some observations in man. *Biological Psychiatry,* 1(3):289–296, 1969.

Winter, C.A., and Flataker, L. Effect of blood plasma from psychotic patients upon performance of trained rats. *A.M.A. Archives of Neurology and Psychiatry,* 80(4):441–449, 1958.

Woolley, D.W. *The Biochemical Bases of Psychoses or the Serotonin Hypothesis About Mental Illness.* New York: John Wiley and Sons, Inc., 1962. pp. 168–170.

Woolley, D.W., and Shaw, E. A biochemical and pharmacological suggestion about certain mental disorders. *Proceedings of the National Academy of Sciences,* 40(4):228–231, 1954.

Wyatt, R.J. Serotonin and sleep. In: Sjoerdsma, A., ed. *Serotonin Now: Clinical Implications of Inhibiting Its Synthesis with Para-chlorophenylalanine.* (Combined Clinical Staff Conference at the National Institutes of Health) *Annals of Internal Medicine,* 73:607–629, 1970.

Wyatt, R.J.; Engelman, K.; Kupfer, D.J.; Scott, J.; Sjoerdsma, A.; and Snyder, F. Effects of *para*-chlorophenylalanine on sleep in man. *Electroencephalography and Clinical Neurophysiology,* 27(5): 529–532, 1969.

Wyatt, R.J.; Fram, D.H.; Kupfer, D.J.; and Snyder, F. Total prolonged drug induced rapid eye movement sleep suppression in anxious-depressed patients. *Archives of General Psychiatry,* 24:145–155, 1971.

Wyatt, R.J.; Fram, D.H.; and Snyder, F. Treatment of intractable narcolepsy with a monoamine oxidase inhibitor (MAOI). (Abstract) *Psychophysiology,* 7:300, 1970.

Wyatt, R.J.; Stern, M.; Fram, D.H.; Tursky, B.; and Grinspoon, L. Abnormalities in skin potential fluctuations during the sleep of acute schizophrenic patients. *Psychosomatic Medicine,* 32(3):301–308, 1970.

Yuwiler, A., and Good, M.H. Chromatographic study of "Reigelhaupt" chromogens in urine. *Journal of Psychiatric Research,* 1(3):215–227, 1962.

Zarcone, V., and Dement, W. Sleep disturbances in schizophrenia, a symposium. In: Kales, A., ed. *Sleep: Physiology and Pathology.* Philadelphia, Pa.: J.B. Lippincott Company, 1969. pp. 192–199.

Zarcone, V.; Gulevich, G.; Pivik, T.; and Dement, W. Partial REM phase deprivation and schizophrenia. *Archives of General Psychiatry,* 18(2):194–202, 1968.

Supplementary References

The following are useful references not listed in the text or in the tables:

Acheson, R.M.; Paul, R.M.; and Tomlinson, R.V. Some constituents of the urine of normal and schizophrenic individuals. *Canadian Journal of Biochemistry and Physiology,* 36(3):295–305, 1958.

Acheson, R.M., and Dearnaley, D.P. Some constituents of the urine of normal and schizophrenic individuals. Part II. *Canadian Journal of Biochemistry and Physiology,* 38(5):503–515, 1960.

Affleck, J.W.; Cooper, A.J.; Forrest, A.D.; Smythies, J.R.; and Zealley, A.K. Penicillamine and schizophrenia—a clinical trial. *British Journal of Psychiatry,* 115(519):173–176, 1969.

Assael, M., and Litiano, D. Levels of glutathione in schizophrenic patients (a biochemical-clinical study). *Diseases of the Nervous* System, 30(10): 680–682, 1969.

Baldessarini, R.J., and Snyder, S.H. Schizophrenia: A critique of recent genetic-biochemical formulations. *Nature,* 206(4989):1111–1112, 1965.

Barbeau, A.; Singh, P.; and Joubert, M. Effect of 3,4-dimethoxyphenylethylamine injections on catecholamine metabolism in rats and monkeys. *Life Sciences,* 5(8):757–767, 1966.

Barbeau, A.; Tétreault, L.; Oliva, L.; Morazain, L.; and Cardin, L. Pharmacology of akinesia—investigations on 3,4-dimethoxyphenylethylamine. *Nature,* 209(5024):719–721, 1966.

Berlet, H.H.; Bull, C.; Himwich, H.E.; Kohl, H.; Matsumoto, K.; Pscheidt, G.R.; Spalde, J.; Tourlentes, T.T.; and Valverde, J.M. Endogenous metabolic factor in schizophrenic behavior. *Science,* 144(3616):311–313, 1964a.

Berlet, H.H.; Pscheidt, G.R.; Spalde, J.K.; and Himwich, H.E. Variations of urinary creatinine and its correlation to tryptamine excretion in schizophrenic patients. *Nature,* 203(4950):1198–1199, 1964b.

Berlet, H.H.; Spalde, J.; Kohl, H.; Bull, C.; and Himwich, H.E. Effects of reduction of tryptophan and methionine intake on urinary indole compounds and schizophrenic behavior. *The Journal of Nervous and Mental Disease,* 140(4):297–304, 1965.

Bindler, E.; Sanghvi, I.; and Gershon, S. Pharmacological and behavioral characteristics of 3,4-dimethoxyphenylethylamine and its N-acetyl derivative. *Archives Internationales de Pharmacodynamie et de Thérapie,* 176(1):1–10, 1968.

Boulton, A.A. The pink spot. *The Lancet,* II(7477): 1362–1363, 1966.

Bourdillon, R.E., and Ridges, A.P. The pink spot. *The Lancet,* I(7434):429–430, 1966.

Bridger, W.H., and Mandel, I.J. The effects of dimethoxyphenylethylamine and mescaline on classical conditioning in rats as measured by the potentiated startle response. *Life Sciences,* 6(7):775–781, 1967.

Brown, D.D.; Silva, O.L.; McDonald, P.B.; Snyder, S.H.; and Kies, M.W. The mammalian metabolism of L-histidine: III. The urinary metabolites of L-histidine-C^{14} in the monkey, human, and rat. *The Journal of Biological Chemistry,* 235(1):154–159, 1960.

Cao, A.; De Virgilis, S.; Lippi, C.; and Trabalza, N. Creatine kinase isoenzymes in serum of children with neurological disorders. *Clinica Chimica Acta,* 23(3):475–478, 1969.

Clarke, C.A., and Sheppard, P.M. Lessons of the "pink spot." *British Medical Journal,* 1(5542):757, 1967.

Creveling, C.R.; Kondo, K.; and Daly, J.W. Use of dansyl derivatives and mass spectrometry for identification of biogenic amines. *Clinical Chemistry,* 14 (4):302–309, 1968.

Crowley, L.V. Creatine phosphokinase activity in myocardial infarction, heart failure, and following various diagnostic and therapeutic procedures. *Clinical Chemistry,* 14(12):1185–1196, 1968.

Daly, J.W.; Axelrod, J.; and Witkop, B. Dynamic aspects of enzymatic *O*-methylation and -demethylation of catechols *in vitro* and *in vivo. The Journal* of *Biological Chemistry,* 235(4):1155–1159, 1960.

Durell, J., and Ryan, J.W. The immune lysis of chicken erythrocytes and its relationship to schizophrenia. In: Walaas, O., ed. *Molecular Basis of Some Aspects of Mental Activity: Proceedings.* Vol. 2. New York: Academic Press, Inc., 1967. pp. 283–302.

Feldman, R., and Dement, W.C. Possible relationships between REM sleep and memory consolidation. Paper presented at Association for Psychophysiological Study of Sleep, Denver, Colo. 1968.

Feldstein, A.; Hoagland, H.; and Freeman, H. On the relationship of serotonin to schizophrenia. *Science,* 128(3320):358, 1958.

Freidhoff, A.J. The pink spot: A red herring? *The Lancet,* II(7474):1188, 1966.

Friedhoff, A.J., and Hollister, L.E. Comparison of the metabolism of 3,4-dimethoxyphenylethylamine and mescaline in humans. *Biochemical Pharmacology,* 15(3):269–273, 1966.

Friedhoff, A.J., and Schweitzer, J.W. An effect of N-acetyldimethoxyphenethylamine. *Diseases of the Nervous System,* 29(7):455–456, 1968.

Gavrila, I.; Iurasog, G.; and Fetuci, M. L'enzymorachie: Etude de l'aldolase et des transaminases du liquide céphalorachidien et du sang dans diverses neuro-infections. *Acta Neurologica et Psychiatrica Belgica,* 68(5):332–344, 1968.

Gershon, E.S., and Shader, R.I. Screening for aminoacidurias in psychiatric inpatients. *Archives of General Psychiatry,* 21(7):82–88, 1969.

Greenberg, R.; Pearlman, C.; Fingar, R.; Kantrowitz, J.; and Kawliche, S. The effects of dream deprivation: Implications for a theory of the psychological function of dreaming. *The British Journal of Medical Psychology,* 43(1):1–11, 1970.

Greiner, A.C., and Berry, K. Skin pigmentation and corneal and lens opacities with prolonged chlorpromazine therapy. *Canadian Medical Association Journal,* 90(11):663–665, 1964.

Hardwick, D.F.; Applegarth, D.A.; Cockcroft, D.M.; Ross, P.M.; and Calder, R.J. Pathogenesis of Methionine-induced toxicity. *Metabolism,* 19(15):381–391, 1970.

Heath, R.G.; Leach, B.E.; and Cohen, M. Relationship of psychotic behavior and abnormal substances in serum. In: Braceland, F., ed. *The Effect of Pharmacologic Agents on the Nervous System.* Vol. 37. Baltimore, Md.: The Williams & Wilkins Company, 1959. pp. 397–411.

Hoffer, A. Adrenolutin as a psychotomimetic agent. In: Hoagland, H., ed. *Hormones, Brain Function, and Behavior.* New York: Academic Press, Inc., 1957a. pp. 181–194.

Hoffer, A. Epinephrine derivatives as potential schizophrenic factors. *Journal of Clinical and Experimental Psychopathology,* 18(1):27–60, 1957b.

Hoffer, A. The action of epinephrine breakdown products on cerebral function. In: Masserman, J.H., ed. *Biological Psychiatry.* Vol. 1. New York: Grune & Stratton, Inc., 1959. pp. 142–152.

Hoffer, A. The effect of adrenochrome and adrenolutin on the behavior of animals and the psychology of man. *International Review of Neurobiology,* 4:307–371, 1962.

Hoffer, A. Schizophrenia as a genetic morphism. *Nature,* 208(5007):306, 1965.

Horodnicki, J. The activity of glycolysis and pentose phosphate pathway in blood cells of schizophrenic patients during phenothiazine drug treatment. Paper presented at the International Congress of Neuropharmacology, 1970. *CINP 7th Congress Abstracts,* Vol. 1. p. 202.

Hughes, B.P. Serum creatine phosphokinase and haemolysis. *Clinica Chimica Acta,* 21(2):287–288, 1968.

Israelstam, D.M.; Sargent, T.; Finley, N.N.; Winchell, H.S.; Fish, M.B.; Motto, J.; Pollycove, M.; and Johnson, A. Abnormal methionine metabolism in schizophrenic and depressive states: A preliminary report. *Journal of Psychiatric Research,* 7(3): 185–190, 1970.

Kurland, H.D., and Fessel, W.J. Distinctive protein patterns in functional psychoses. *Proceedings of the Society for Experimental Biology and Medicine,* 113(2):249–251, 1963.

Kuznetzova, N.I., and Semenov, S.F. Detection of antibrain antibodies in the blood serum of patients with neuropsychiatric diseases. *Zhurnal Nevropatologii i Psikhiatrii imeni S.S. Korsakova,* 61:869–874, 1961.

LeBlanc, J. Response to histamine in mental patients before and after tranquilizer therapy. (Abstract) *Biological Pharmacology,* 8(1):152, 1961.

Lingjaerde, P.S. Carbohydrate metabolism in schizophrenia. *International Review of Neurobiology,* 11:259–290, 1968.

Lozovsky, D.V. The biochemical investigations of schizophrenia in the U.S.S.R. *International Review of Neurobiology,* 11:199–225, 1968.

McGeer, P.L., and McGeer, E.G. Aromatic urinary excretion in schizophrenics. In: Folch-Pi, J., ed. *Chemical Pathology of the Nervous System.* New York: Pergamon Press, Inc., 1961. pp. 589–599.

McIsaac, W.M. A biochemical concept of mental disease. *Postgraduate Medicine,* 30(2):111–118, 1961.

Mattke, D.J., and Adler, M. Investigation on the mode of action of D-penicillamine in chronic schizophrenia. Paper presented at the International Congress of Neuropharmacology, 1970.

Mattock, G.L.; O'Reilly, P.O.; and Hughes, G. Detection of a characteristic substance in the urine of schizophrenics. *Diseases of the Nervous System,* 28(6):405–406, 1967.

Nicolson, G.A.; Greiner, A.C.; McFarlane, W.J.G.; and Baker, R.A. Effect of penicillamine on schizophrenic patients. *The Lancet,* I(7433):344–347, 1966.

Price, J. and Hopkinson, G. Mono-amine oxidase inhibitors and schizophrenia. *Psychiatrica Clinica,* 1(2):65–84, 1968.

Price, J.; Ridges, A.P.; Bourdillon, R.E.; and Harper, P. Pink spot as an indicator of prognosis in schizophrenia. *Acta Psychiatrica Scandinavica,* 43 (4): 424–431, 1967.

Reynolds, E.H. Schizophrenia-like psychoses of epilepsy and disturbances of folate and vitamin B_{12} metabolism induced by anticonvulsant drugs. *The British Journal of Psychiatry,* 113(501):911–919, 1967.

Ridges, A.P., and Bourdillon, R.E. Schizophrenia, transmethylation and pink spot. *Proceedings of the Royal Society of Medicine,* 60(6):555–557, 1967.

Ryan, J.W.; Brown, J.D.; and Durell, J. Antibodies affecting metabolism of chicken erythrocytes: Examination of schizophrenic and other subjects. *Science,* 151(3716):1408–1410, 1966.

Ryan, J.W.; Brown, J.D.; and Durell, J. Concordance between two methods of assaying the plasma effects on chicken erythrocyte metabolism. *Journal of Psychiatric Research,* 6(1):45–49, 1968.

Schweitzer, J.W., and Friedhoff, A.J. The metabolism of *a*-^{14}C-3,4-dimethoxyphenethylamine. *Biochemical Pharmacology,* 15(12):2097–2103, 1966.

Schweitzer, J.W., and Friedhoff, A.J. The metabolism of dimethoxyphenethylamine, a compound found in the urine of schizophrenics. *American Journal of Psychiatry,* 124(9):1249–1253, 1968.

Semenov, S.F. The study of autoimmune processes in a psychiatric clinic. *International Review of Neurobiology,* 11:291–328, 1968.

Senoh, S.; Daly, J.; Axelrod, J.; and Witkop, B. Enzymatic *p*-O-methylation by catechol O-methyl transferase. *Journal of the American Chemical Society,* 81(23):6240–6245, 1959.

Shchirina, M.G., and Vartanyan, M. Clinicobiological research in schizophrenia in the Soviet Union. *Proceedings of the Royal Society of Medicine,* 61:943–947, 1968.

Shopsin, B., and Gershon, S. The effects of sera from psychiatric patients on guinea pig brain respiration. *The Journal of Nervous and Mental Disease,* 148(2):188–191, 1969.

Silva, F.; Heath, R.G.; Rafferty, T.; Johnson, R.; and Robinson, W. Comparative effects of the administration of taraxein, d-LSD, mescaline, and psilocybin to human volunteers. *Comprehensive Psychiatry,* 1(6):370–376, 1960.

Smith, P. Metabolism of dihydroxyphenylalanine in human subjects. *Nature,* 213(5078):802–803, 1967.

Solomon, G.F., and Moos, R.H. Emotions, immunity, and disease: A speculative theoretical integration. *Archives of General Psychiatry,* 11(6):657–674, 1964.

Spiro, H.R.; Schimke, R.N.; and Welch, J.P. Schizophrenia in a patient with a defect in methionine metabolism. *The Journal of Nervous and Mental Disease,* 141(3):285–290, 1965.

Sprince, H. Indole metabolism in mental illness. *Clinical Chemistry,* 7(3):203–230, 1961.

Sprince, H. Biochemical aspects of indole metabolism in normal and Schizophrenic subjects. *Annals of the New York Academy of Sciences,* 96(1): 399–418, 1962.

Sprince, H.; Parker, C.M.; Jameson, D.; and Josephs, J.A., Jr. Effect of methionine on nicotinic and indoleacetic acid pathways of tryptophan metabolism *in vivo. Proceedings of the Society for Experimental Biology and Medicine,* 119(4):942–946, 1965.

Tanimukai, H.; Ginther, R.; Spalde, J.; Bueno, J.R.; and Himwich, H.E. Psychotogenic N,N-dimethylated indole amines and behavior in schizophrenic patients. *Recent Advances in Biological Psychiatry,* 10:6–15, 1968.

Udenfriend, S.; Witkop, B.; Redfield, B.G.; and Weissbach, H. Studies with reversible inhibitors of monoamine oxidase: Harmaline and related compounds. *Biochemical Pharmacology,* 1(2):160–165, 1958.

Vogel, W.H. Biochemische Untersuchungen bei Schizophrenie. Über das "Pink Spot"-phanomen, *Münchener Medizinische Wochenschrift,* 109(31): 1633–1641, 1967.

Vogel, W.H., and Ahlberg, D. A rapid procedure for the separation and determination of 3,4-dimethoxyphenylethylamine. *Analytical Biochemistry,* 18 (3):563–566, 1967.

Vogel, W.H.; Ahlberg, C.D.; Di Carlo, V.; and Horwitt, M.K. Pink spot, *p*-tyramine and schizophrenia. *Nature,* 216(5119):1038–1039, 1967.

Richard J. Wyatt, M.D., is a research psychiatrist at the Laboratory of Clinical Psychopharmacology, NIMH, St. Elizabeths Hospital, Washington, D.C.; Benedict A. Termini, M.D., is a medical intern at Mercy Hospital, Baltimore, Md.; and John Davis, M.D., is Professor of Psychiatry and Associate Professor of Pharmacology at Vanderbilt University, Nashville, Tenn.