(1965) investigated a patient with 48 hour manic depressive cycles and found low urine 17 hydroxy-corticosteroids during the manic days and high levels during the depressed days. Longitudinal studies in patients with manic depressive psychosis have shown lower cortisol secretion in the manic state and hypersecretion during depression (Ettigi & Brown, 1977). As far as the dexamethasone suppression test is concerned, patients in the manic or hypomanic phase do not usually exhibit non-suppression or early escape from suppression (Carroll, 1982). We wondered if manic patients would show a prolonged suppression of cortisol in response to dexamethasone.

Eleven manic patients and 12 schizophrenic patients without prominent affective features formed the subjects of the study. All patients satisfied the appropriate DSM III criteria. Conditions likely to interfere with DST were excluded. Blood was drawn for baseline plasma cortisol estimation at 11.30 p.m. prior to the administration of 0.5 mg of dexamethasone orally. It was decided to use this smaller dose of dexamethasone to accentuate any difference between the two groups. Blood samples were drawn at 11.30 p.m. on day II and 8.00 a.m. and 11.30 p.m. on day III. Plasma cortisol was estimated using the radio immuno assay technique. Two of the manic patients were given barbiturates during the period of DST and had to be excluded from the study. All the other patients were on various anti-psychotic drugs and two patients (one manic and one schizophrenic) were on small doses of orphenadrine hydrochloride. All the manic patients remained in a manic state for at least one week after the DST was completed. A baseline cortisol level of less than 2 μgm/DL was considered to be below normal and patients with post-dexamethasone cortisol levels of less than 6 μgm/DL were considered to show suppression.

Two out of nine manic patients and five out of twelve schizophrenic patients showed baseline cortisol value. There was no significant difference in the proportion of patients showing suppression between the two groups on any of the three post-dexamethasone cortisol assays ($P = 0.714$; $P = 0.429$; $P = 0.414$ respectively—Fischer's Exact Test). In view of the problems involved in the interpretation of changes of cortisol values following the administration of dexamethasone in patients who prior to the administration showed low cortisol values, the analysis was repeated using only those cases whose baseline values were normal or high (seven manics and seven schizophrenics). No significant differences were found between the two groups.

Amongst the difficulties in interpreting the data are the small sample size and the absence of normal controls. It is interesting to note that the only patient who showed a suppressed cortisol level (following dexamethasone administration) on day III at 8.00 a.m., a time when a cortisol spurt would normally be expected, was a manic who showed a higher than normal midnight baseline cortisol level. This makes us wonder if any prolonged post-dexamethasone cortisol suppression might exist only in the manics who show an elevated (above normal) midnight baseline cortisol and whether this might be best studied by measuring the 8.00 a.m. post-dexamethasone cortisol levels.

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NEUROLEPTIC MALIGNANT SYNDROME AND HEART STROKE

Dear Sir,

Dr Singh (*Journal*, July 1984, **145**, 98), in his discussion of neuroleptic malignant syndrome, makes the erroneous assertion that loss of consciousness and absence of sweating are classic signs of this disorder. Though confusion and altered consciousness are frequently mentioned in reported cases (Caroff, 1980), actual loss of consciousness is not commonly found. Rather than an absence of sweating, a profuse diaphoresis is usually seen (Caroff, 1980; Smego & Durack, 1982; Ayd, 1983; Szabadi, 1984). In the case presented by Singh, the abrupt loss of consciousness coupled with an elevated temperature and an absence of sweating on an "unusually hot" day, suggest that the patient suffered from heat stroke, not NMS. Neuroleptics may contribute to heat stroke by inhibiting the sweating mechanism (Smego & Durack, 1982). Though rigidity, which was present in this case, is not a common feature of heat stroke, it is a common side effect of neuroleptic use and therefore should not deter the clinician from entertaining this diagnosis when the appropriate signs are present. Also, a more comprehensive presentation of data such as CPK, WBC count,

electrolytes, and BUN would have given a clearer understanding of this case.

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CIRCADIAN RHYTHMS AND PSYCHIATRY

DEAR SIR,

We wish to offer the following remarks on Christopher Thompson's article on "Circadian Rhythms and Psychiatry" (*British Journal of Psychiatry*, **145**, 204–206). The review does not mention any of the recent studies on the circadian rhythm of melatonin in depression. Research on melatonin rhythm in affective disorders is being pursued actively by many investigators. Wetterberg and his colleagues in Sweden (1982) hypothesised that a low melatonin secretion is a specific neuroendocrine disturbance and may be a genetic marker for affective disorders. Lewy and coworkers (1984) have been studying melatonin rhythm in affective disorders as a marker for human circadian rhythms entrained to light. We share the view of Lewy and have hypothesised that melatonin rhythm in depression is an index of a disturbance of a central pacemaker system which is normally entrained to environmental photoperiod. It is our contention that the diverse dysrhythms in depression may be related to a disturbance in a central neural mechanism. We use plasma melatonin rhythm as a measurable index of its central pacemaker activity, since the stability and usefulness of human melatonin rhythm as a marker has been well established.

Studies on circadian rhythms will be more meaningful when interpreted with respect to a vital entraining cue or Zeitgeber, to infer a true change in their phase (phase advance or delay), rather than when the phase angle between the different rhythms alone is investigated. These have been done using the Phase Response Curves (PRC). PRC's for animals (activity-rest cycles in relation to light) and for man (melatonin rhythm and REM latency in relation to light) have been found to be similar with an advance portion in the morning and a delay portion in the evening (Lewy, 1984).

Our studies (Nair *et al*, 1984) show that under constant and uniform conditions of environmental day length, the depressive patients show a delayed onset of melatonin rhythm compared to matched controls. This raises the possibility that there are at least some depressives who have phase-delayed circadian rhythms. This is supported by Lewy's recent proposition that there may be two subgroups of depressives, with phase-advanced or phase-delayed rhythms (Lewy *et al*, 1984). Studies on cyclical symptoms such as early morning waking in relation to the phase changes in melatonin rhythm are being done.

Our data on a few normal volunteers show that lithium delays the secretory offset of melatonin in response to light, while it does not affect the onset of the rhythm *per se* (Nair & Hariharasubramanin, 1984). This selective effect of lithium on the suppressant effect of light, without affecting the entraining influence of light is interesting and the investigations are being continued.

We may also mention that circadian rhythm research in depression, specifically relating to an environmental Zeitgeber, will be useful to bring out the level of plasticity and adaptability of the central nervous system to the environment.

Thus, studies on circadian rhythm of human plasma melatonin in relation to photoperiod are worthy of greater attention towards identifying the basic mechanisms involved in disturbances of circadian rhythms in affective disorders.

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