ELEVATED MELATONIN SERUM CONCENTRATIONS IN PSYCHIATRIC PATIENTS TREATED WITH CHLORPROMAZINE

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The role of the human pineal gland in normal physiology and in disease is little understood. An active metabolite, melatonin, is thought to exert an inhibitory influence on the pituitary-gonadal axis (Minneman & Wurtman, 1975) and also to control cyclic variations in sleep and arousal (Quay, 1974). Melatonin synthesising enzymes exhibit a diurnal rhythm, both in rat (Axelrod & others, 1965: Klein & Weller, 1970) and in man, and is synchronous with the serum melatonin diurnal rhythm (Smith & others, 1977). Transmethylation by pineal hydroxyindole-o-methyl transferase (HIOMT) might, if defective, be implicated in the pathogenesis of abnormal mental states (Jones & others, 1969: Greiner, 1970). Psythiatric patients often show disturbances in sleep patterns (Reich, 1975; Jus, 1973). We used radioimmune assay (Smith & others, 1977) to estimate the elevation of daytime melatonin (and possibly nighttime) serum concentrations in 5 psychiatric patients being treated with varying doses of chlorpromazine (100mg-400mg daily) who thus produced high concentrations with little rhythm (Table 1). The daytime concentrations were enhanced 4-5 times over normal whilst the nighttime increase was $1\frac{1}{2}$ times normal. A similar effect was reported in rats (Wurtman & others, 1968) when chlorpromazine increased serum melatonin concentration five-fold. Five psychiatric patients not being treated with chlorpromazine had lower than normal serum melatonin concentrations (Table 1), suggesting that the increase in melatonin serum concentrations in patients with abnormal mental states is due to the effect of the drug and not to an inherent difference from normal individuals. However, no dose response correlation can yet be made. Whether this effect of chlorpromazine is due to an increased biosynthesis of melatonin or a reduced rate of metabolism is unclear. But, since intravenous injection of melatonin in man induces sleep (Cramer & others, 1976) the elevated melatonin concentrations can explain the initial tranquillizing effect observed in the clinical use of chlorpromazine before the gradual onset of the antipsychotic action. Interestingly fluphenazine, another neuroleptic, does not appear to increase serum melatonin concentrations in man or in the rat (unpublished data). Whether the low absolute levels of serum melatonin (and shallow rhythm) in the group of patients not being treated with chlorpromazine is significantly different from normal has yet to be established.

Table 1. Human Serum Melatonin Levels through 24 hours (pg/ml) $\pm$ s.d.

Normal male (5)	1000	1400	1800	2200	0200	0600 h
average age 35 (26-48)	28(±9)	20(±6)	25(±8)	47(±22)	78(±25)	51(±7)
Psychiatric male (5)	1100	1500	1900	2300	0300	0700 h
average age 35 (17-47)	79(±12)	110(±29)	123(±32)	134(±43)	122(±34)	102(±34)
on chlorpromazine 100mg-400mg daily)						
Psychiatric male (5)	1000	1400	1800	2200	0200	0600 h
average 41(36-62)	13(±5)	12(±2)	16(±4)	19(±6)	26(±10)	22(±8)
not on chlorpromazine						

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