EFFECTS OF DIFFERENT LIGHT CYCLES AND STRESS ON URINARY EXCRETION OF MELATONIN AND TUMOR SPREAD IN MICE BEARING LEWIS LUNG CARCINOMA.

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Melatonin is an indole compound secreted by the pineal gland. In humans and in animals this hormone shows a circadian rhythm with a nocturnal peak and a diurnal abolition of melatonin plasmatic levels. Melatonin appears to be involved in various biological functions among which the regulation of the neuroendocrine and immune system, and of cellular mitosis appear of relevance. In this connection, melatonin has been studied for its possible implications in the control of neoplastic growth; moreover, available data indicate that stress influences tumor growth and metastasis by means of modulation of antitumor host responses via neuroendocrine mechanisms among which melatonin is also involved (1). It seemed therefore interesting to examine the relationships between the urinary levels of melatonin induced by different light cycles tumor growth and metastasis as a function of stress (spatial disorientation) in mice bearing Lewis lung carcinoma. The animal used are young BD2F1 female mice, which were kept 5 per cage in order to avoid the effects of overcrowding or isolation on tumor progression. The cages were placed in a protected housing for 2 weeks before tumor inoculation to allow the animals to recover from the stress of shipment and to adapt them to the housing conditions and light cycles. The light cycles in the cabinet were 12/12, 16/8 and 24/0 (light/dark h/h) with an intensity of 2100 lux in the cages; tumor transplantation and evaluation were performed as already described. The protected housing consisted of a cabinet containing the animal cages with laminar air flow, minimizing acoustic, olfactory and visual communication among the cages, and also with events outside of the cabinet. The cabinets were contained in a room distant from other animal rooms, where staff entered only once every 5 days for water and food supply to the animals. Stress, i.e. spatial disorientation (SD), was applied to the animals by spinning the cages at 45 rpm for 10 min every hour from time of tumor inoculation until sacrifice. These experimental conditions have been already described (2). The results in Table 1 show that nocturnal plasmatic levels of melatonin are consistently higher than those during light hours; nocturnal melatonin levels are further markedly and significantly increased by stress (SD). At the same time,

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metastasis weight is significantly reduced.

Table 1. Effects of different light cycles and stress on urinary excretion of melatonin and tumor spread in mice bearing Lewis lung carcinoma.

SD	LIGHT/ DARK CYCLES	URINARY MELATONIN EXCRETION (pg) LIGHT	DARK	TUMOR WEIGHT (G)	METASTASIS NUMBER	METASTASIS WEIGHT(mg)
-	16/8	5.3±1.6	48.9±18.0○	2.7±0.2	39.4±4.9	210.4±27.4■
+	16/8	6.4±1.3	76.0± 5.0○	3.0±0.2	35.6±3.1	150.5±20.5
-	12/12	6.4±2.4	68.9±17.0○	3.6±0.3	36.9±4.4	167.4±26.4
+	12/12	6.0±2.1	92.0±21.0○	3.2±0.4	26.4±2.9	107.4± 9.8□△
-	24/0	6.6±1.5[@]	46.8±15.3[&]○	3.1±0.3	44.8±5.7	219.1±37.7▲
+	24/0	6.8±2.1[@]	152.0±20.0[&]●	2.8±0.3	29.1±5.2	95.1±22.4□△

Melatonin was determined by a radioimmunoassay (RIA-2Ab Nuclear Medica, Italy) on day 15 ([@]: 8 a.m. - 8 p.m.; [&]: 8 p.m. - 8 a.m.). Student-Neumann-Keuls test, $p<0.05$, ○:means significantly different from ●; □: means significantly different from ■ ; △:means significantly different from ▲.

This finding indicates a participation of melatonin in the regulation of the process of metastasis formation, with a protective role of this hormone; this result is consistent with a reported increase of tumor metastasis in mice after surgical pinealectomy (3).

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