PINEAL GLAND FUNCTION DURING THE REPRODUCTIVE CYCLE - A MULTI SPECIES STUDY

by

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SUMMARY

1) The thesis concerns a study of pineal gland function during the reproductive cycle of several species including the sheep, human and a scincid lizard Tiliqua rugosa.

2) The development and validation of a reliable radioimmunoassay for the presumptive pineal hormone melatonin is described and its application to the measurement of melatonin content of pineal tissue and blood plasma to provide an index of pineal function investigated.

3) Studies in the sheep and humans confirmed that plasma melatonin levels were higher during periods of darkness than during periods of light. The increase in plasma levels of melatonin was associated with the onset of darkness. In the sheep no relationship was apparent between this pattern of melatonin secretion and circulating levels of cortisol and tryptophan.

4) In the ewe there were no consistent alterations in circulating plasma melatonin which could be related to the stage of the oestrous cycle. Removal of the ovaries had no consistent effect on either the daytime concentrations of plasma melatonin or the diurnal rhythm. Depot injections of a synthetic progestin (medroxyprogesterone) had no significant effect on daytime concentrations of plasma melatonin in ovariectomised sheep, however, daily injection of oestradiol 17β raised the daytime plasma melatonin concentrations in some animals for the period of the injections.

5) Pregnancy was associated with alteration in the diurnal rhythm of maternal plasma melatonin in the sheep but not in the human. The nyctohemeral rise in plasma melatonin content of pregnant ewes of 90-150 days gestation was reduced. By contrast, plasma melatonin concentrations continued to exhibit a diurnal rhythm in the pregnant women.

6) Studies on foetal sheep showed that the pineal had an increased capacity to synthesise melatonin during the last 4-5 days of gestation. This increased synthetic capacity is associated with increased pineal gland content of melatonin but is not associated with increased plasma concentrations. Infusion of synthetic corticotrophin into the foetus induced parturition but did not cause any detectable changes in plasma melatonin concentrations. Infusion of melatonin (1-4 ug/hr) into the foetal circulation did not interfere with either synthetic corticotrophin induced parturition or normal parturition. By use of radioactive tracer substances it was shown exogenously administered melatonin can transfer from the maternal circulation across the placenta to the foetus. The reverse situation can also occur.

7) Plasma melatonin concentrations were monitored in pinealectomised sheep. An immunoreactive substance probably melatonin was detected in all sheep, often at concentrations greater than 200 pg/ml. Pinealectomised sheep did not show a diurnal rhythm in plasma melatonin. Plasma melatonin in sham operated and pinealectomised pregnant ewes was low and no changes in concentration appeared before or during parturition.

8) Plasma concentrations of melatonin were investigated in response to alterations in photoperiod and parietalectomy in the scincid lizard Tiliqua rugosa. A diurnal rhythm in plasma melatonin was discovered. Highest levels occurred during darkness. Peak melatonin concentrations tended to be lower during the breeding season. Shifting the photoperiod 6 hours and 12 hours resulted in a shift in the diurnal rhythm. Constant light and constant darkness abolished the diurnal rhythm. Parietalectomy had no significant depressive effect on the diurnal rhythm of plasma melatonin unless it was accompanied by shielding of the lateral eyes.

9) Analysis of plasma melatonin in rats, cattle, donkeys, chickens, camel and pig showed that nighttime concentrations were higher than daytime concentrations.

10) A study of pineal gland enzymes in the Tammar Wallaby indicated that a significant decrease in melatonin synthesis occurred at the time of blastocyst activation in free ranging animals. By contrast, very low concentrations of melatonin were apparent in possum pineal tissue and blood at different times of the year. No diurnal rhythm was evident.

11) During the course of investigations, two patients with radiographically identified pinealomas were investigated for anomalies in plasma melatonin content. Melatonin was undetectable at all times. Plasma gonadotrophins were in one case abnormally low (S.D.) while in the other case they were normal (E.S.). Prolactin levels were abnormally high (S.D.) and abnormally low (E.S.). Plasma corticoid levels were within normal limits.