

The time of steroid therapy

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Physicians have become aware that evening doses of corticosteroids cause more adreno-pituitary suppression (Di Riamando & Forsham, 1956). There is an increasing trend for physicians to give corticosteroid therapy as a once daily morning dose, or as alternate day therapy.

Recent investigations by our group have demonstrated circadian variations in cell-mediated immune responses in the rat (Knapp & Pownall, 1977). We have analysed the time of onset of change in renal function, due to acute rejection, in fifty patients following a renal transplant, and find this is most frequently at night. This is also the time when humans show the maximum cell-mediated immune response to Heaf testing (Cove-Smith, Kabler, Pownall & Knapp, 1978).

Analysis of rejection episodes in the fifty transplanted patients shows that a rejection episode most commonly affects renal function 6-8 days after the onset of graft function (twenty of thirty rejections occurring in the first 10 days), and that there is an increased probability of rejection around 7 days after a previous episode (the interval between rejections being 5-7 days in thirty-five pairs of rejection episodes out of fifty-six pairs separated by less than 14 days). These results confirm those of de Vecchi, Halberg, Sothorn, Cantaluppi & Ponticelli (1978).

These studies suggest that more thought should be given to the time when a treatment will favourably influence a pathological process. Timing of therapy to match the biological rhythmicity of a pathological process may result in more effective prophylaxis or treatment.

Prescribing patterns for immunosuppressive therapy in fourteen British Transplant Units have been studied, and show a wide range of policy, for example—prednisolone is given twice daily by six, three times daily in one, once daily in the morning by two, once daily in the evening by two, on alternate days in another and in a variable way in two. Azathioprine may be taken once, twice or three times daily depending on the unit. This range of policy reflects medical uncertainty about the optimum time for administration.

References

- COVE-SMITH, J.R., KABLER, P., POWNALL, R. & KNAPP, M.S. (1978). Circadian variation in an immune response in man. *Br. med. J.* (in press).
- DE VECCHI, A., HALBERG, F., SOTHERN, R.B., CANTALUPPI, A. & PONTICELLI, C. (1978). Circaseptan rhythmic aspects of rejection in treated patients with kidney transplants. *Proc. Int. Symp. on Chronopharmacology*. Ed. Walker, C. (in press).
- DI RIAMANDO, V.C. & FORSHAM, P.H. (1956). Some clinical implications of the spontaneous diurnal variation in adrenal cortical secretory activity. *Am. J. Med.*, **21**, 321-323.
- KNAPP, M.S. & POWNALL, R. (1977). Circadian variations in delayed hypersensitivity to a contact sensitizing agent. *J. Physiol.*, **276**, 42-43.