

Suppression of DTH mediated by cloned helper T cells with ciclosporin and dexamethasone

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Introduction

DTH is an immunologically specific inflammatory reaction maximal at 24–48 h, with a characteristic histological appearance of infiltration with mononuclear cells [1]. This study evaluates the ef-

fects of two drugs in a DTH reaction mediated by cloned helper T cells and in a model of footpad swelling induced by a lymphokine-containing supernatant. The two drugs tested were Ciclosporin (Cs), which acts selectively on T lymphocytes, and Dexamethasone (Dex), which

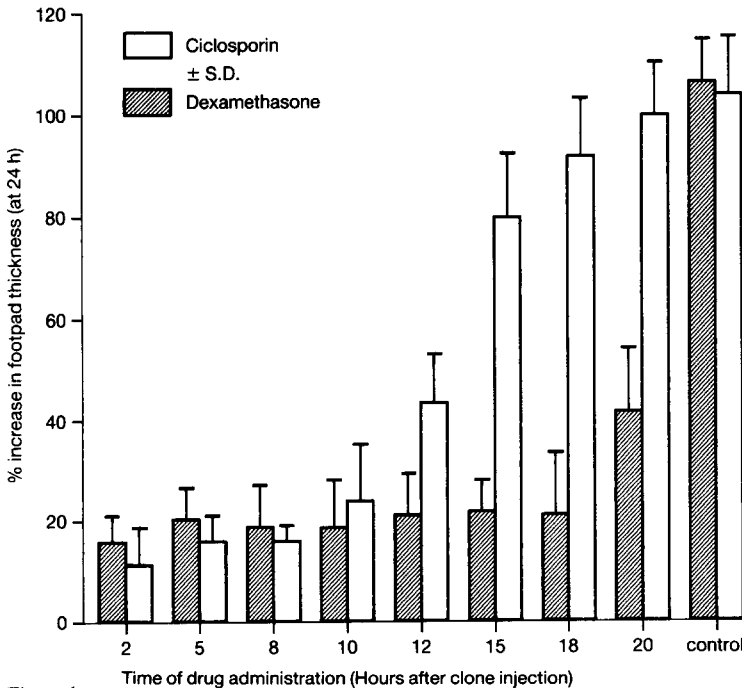


Figure 1

Time dependence of drug administration for inhibition of DTH. The DTH reaction was induced as described under Methods. Cs

(90 mg/kg) or Dex (0.5 mg/kg) was given orally at different times after injection of the clone.

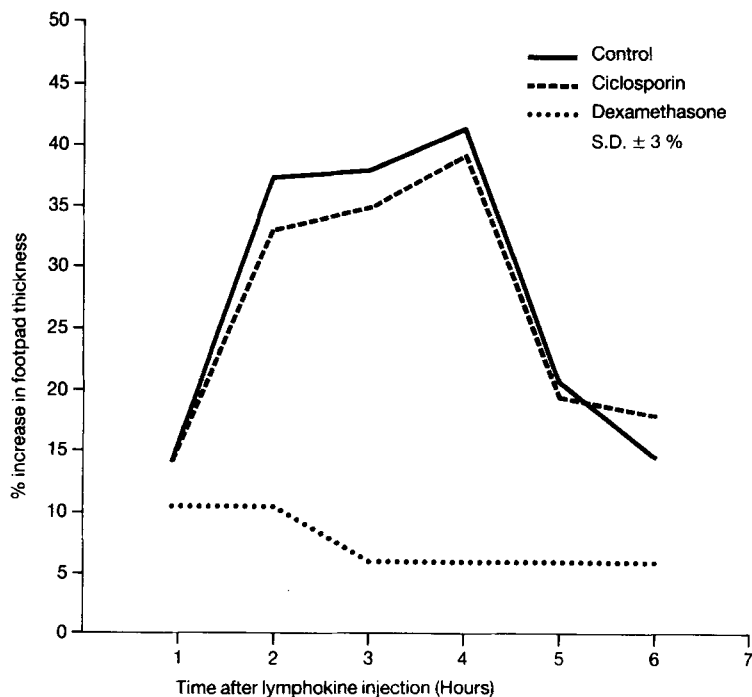


Figure 2

Drug effect on lymphokine-induced swelling. Lymphokines, obtained by *in vitro* stimulation of cloned helper T cells with SRC,

were injected s.c. into one hind footpad. Drugs were given 1 h before lymphokine injection.

exerts an immunosuppressive as well as an anti-inflammatory effect.

Methods

C57 BL/6J mice were injected s.c. with 5×10^4 cloned helper T cells together with sheep erythrocytes (SRC) in one hind footpad and with the same clone plus an unrelated antigen as control in the other [2]. A single dose of Cs (90 mg/kg) or Dex (0.5 mg/kg) was given orally at different times after injection of the clone.

In a second experiment the T cell clone was stimulated *in vitro* with SRC over a period of 24 h, in the presence of I-A-compatible macrophages. The resultant lymphokines present in the supernatant were injected s.c. into one hind footpad of C57 BL/6J mice. A control supernatant was obtained from the same T cell clone incubated without SRC, and injected into the other hind footpad. Drugs were given 1 h before lymphokine injection.

Footpad thickness was measured as indicated.

Results and conclusions

The inhibitory effect of a single dose of Cs or Dex was tested in a DTH reaction mediated by cloned helper T cells (Fig. 1) and in a model of lymphokine-induced footpad swelling (Fig. 2).

Cs, given up to 10 h after sensitization, completely abolished the response, but had no effect when given after 15 h. In contrast Dex still inhibited the response after 20 h.

The lymphokines induced swelling within 2 h. Dex, but not Cs, blocked this swelling.

These results are consistent with the concept that Cs inhibits the production of lymphokines but, unlike Dex, does not alter their effects once they are produced.

References

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- [2] A. T. J. Bianchi, H. Hooijkaas, R. Benner, R. Tees, A. A. Nordin and M. H. Schreier, *Clones of helper T cells mediate antigen specific, H-2 restricted DTH*. Nature 290, 62-63 (1981).