66. FLUID FORMATION AND CYTOKINE EXPRESSION IN THE NORMAL AND INFLAMED RAT TESTIS FOLLOWING LEYDIG CELL DEPLETION

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Leydig cells play an important role in several inflammation-related responses of the testis, stimulating testicular macrophage recruitment, producing the inflammatory cytokines interleukin-1 (IL-1) and IL-6, and regulating interstitial fluid (IF) formation through an androgen-dependent mechanism mediated via the seminiferous tubules. In contrast to other tissues, inflammation in the testis results in a reduction in IF formation. A similar decline in IF follows withdrawal of testosterone (T). In the present study, adult male rats received the Leydig-cell-specific toxin, ethane dimethane sulphonate (EDS; 75 mg/kg i.p.) or carrier alone. Seminiferous tubule function was supported in some EDS-treated animals by 24 cm subcutaneous T-implants. After 10 days, animals received an inflammatory stimulus, lipopolysaccharide (LPS; 0.1 mg/kg i.p.) or saline and were killed 3 h later. Testes were collected for measurement of cytokine mRNA by RNase protection assay (RiboQuant^{TM}), IF volume and testicular T levels. Both depletion of Leydig cells by EDS and LPS-treatment caused a decrease in IF to about 35% of control, but the effects were not additive. Maintenance of T prevented the IF decrease following EDS-treatment, but not the LPS-induced effects. Transforming growth factor-β1 (TGFβ1), migration inhibitory factor (MIF) and interferon-γ (IFNγ) were strongly expressed in the normal and inflamed testis, whereas other cytokines (IL-1α, IL-1β, IL-1ra, TNFα, IL-6 and IL-10) were close to or below the limit of detection in all groups. EDS caused a significant decline in TGFβ1, MIF and IFNγ expression, which was prevented by the T-implants. These data indicate (i) that testis expression of TGFβ1, MIF and IFNγ is not dependent on intact Leydig cells, but is under T control, and (ii) the decline in testicular IF during inflammation involves the Leydig cells, but this regulation is T-independent (i.e. mediated by non–androgenic Leydig cell secretions).

10.1071/SRB03Ab66