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JOURNAL ARTICLE

Leydig cell apoptosis in response to ethane dimethanesulphonate after both in vivo and in vitro treatment

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The biological effects of ethane dimethanesulphonate (EDS) are unique since cytotoxicity in the adult rat is almost exclusively confined to the Leydig cells. For this reason, EDS has been used extensively to investigate the physiological role of the Leydig cell and its products. Experiments were conducted to determine whether the Leydig cell will undergo apoptosis in response to EDS or methylprednisolone (MP), a glucocorticoid known to cause apoptosis in a number of other cell types. Percoll-purified Leydig cells were incubated for 24 hours with EDS (750 micrograms/ml), at which time the cells attached to the culture plate became rounded up while control cells were flattened and polyhedral. Following incubation with EDS or MP (10 micromM), cells that became detached from the plate were characteristically apoptotic when stained with the fluorescent DNA dye, acridine orange. These cells had shrunk and the nuclear chromatin had become condensed, which is an early characteristic of apoptosis in other cells; eventually, apoptotic bodies formed, reflecting a later apoptotic stage. Electrophoresis of DNA extracted from the treated Leydig cells exhibited the characteristic ladder of the apoptotic process. Increasing the concentration of EDS or MP resulted in a dose-dependent increase in the incidence of apoptosis that reached a maximum of 25% (EDS) or 12% (MP) of detached cells. Administration of EDS in vivo caused a 20-fold increase in the number of apoptotic cells observed in interstitial cell preparations. In conclusion, the data indicates that programmed cell death, apoptosis, can occur in the Leydig cell and that this is the likely mechanism by which EDS kills the cells in vivo and in vitro.

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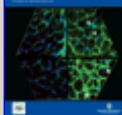
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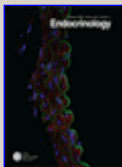
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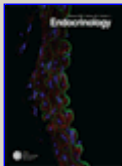


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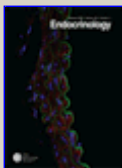


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