COMMENTS

Glucocorticoids Decrease Survival of Immature Human B Cells *In Vitro*

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The efficacy of glucocorticoids for the treatment of inflammatory, allergic, and autoimmune diseases, as well as preventing rejection of transplanted organs, is widely recognized. Laboratory and clinical studies during the past 50 years have shown that judicious consideration of dose and regimen is required to balance the suppression of activated immune cells responsible for the disorder while maintaining adequate function to defend against infections (1, 2). Numerous studies have demonstrated that T lymphocyte-dependent activities in rodent models, non-human primates and humans are particularly impaired by elevated glucocorticoid levels. While the impact of glucocorticoids on human B cells has remained somewhat unclear, a series of reports by Fraker and associates during the past decade have shown that synthetic and endogenous glucocorticoids induce losses of murine precursor B, as well as precursor T, cells both *in vitro* and *in vivo* (3, 4). The report by Lill-Elghanian et al. (5) selected as the Best Paper Award in the Clinical/Preclinical and Translational Category for 2002 provides the first evidence that the *in vitro* effects of glucocorticoids on human B lineage cells from bone marrow parallel the sensitivity of the murine B cell lineage.

Mononuclear cells isolated from bone marrow aspirates from 22 subjects were exposed to physiologic levels of dexamethasone and cortisol *in vitro*. Mean survival of CD19 cells in cultures containing 1 μM dexamethasone was 67% that in control cultures. However, the impact of the synthetic glucocorticoid on cells from subjects varied markedly ranging from very sensitive (40–50% loss of CD19+ cells in presence of 1 μM dexamethasone for 20 h) to resistant (less than 20% decrease in survival). This difference in responsiveness was independent of age and gender, and donors were not receiving medications expected to confound the effect of the *in vitro* exposure. Additional studies using cells from several donors revealed that cortisol was only slightly less potent than dexamethasone in inducing the *in vitro* loss of CD19 cells, and that pro- and pre-B cells were considerably more sensitive to the glucocorticoids than mature B cells. Phenotypic analysis of the B cell population revealed that the variable survival response of CD19 cells from different donors when exposed to dexamethasone was likely due to differences in the relative percentages of immature and mature cells in the cultures. Finally, preliminary experiments suggest that the glucocorticoids mediate their affect on immature human B cells by accelerating apoptosis as previously reported for pro- and pre-B cells from murine bone marrow.

In light of the widespread use of glucocorticoid therapy and the numerous conditions that are known to induce chronic elevation of plasma cortisol, the observations of the Fraker research team provide the impetus for evaluating the possible effects of synthetic and natural glucocorticoids on B cell survival, development and activity *in vivo*.

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