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Fauci A S, Dale D C & Balow J E. Glucocorticosteroid therapy: mechanisms of action and clinical considerations. *Ann. Intern. Med.* **84**:304-15, 1976.
[Clinical Physiology Sect., Lab. Clinical Investigation, Natl. Inst. Allergy and Infectious Dis., Bethesda, MD, and Univ. Washington Sch. Med., Seattle, WA]

Glucocorticoids suppress inflammation by a number of diverse effects on circulating white blood cells. They cause neutrophilic leukocytosis together with eosinopenia, monocytopenia, and lymphocytopenia. Therapeutic corticosteroid regimens can be formulated based on an understanding of their diverse effects on inflammatory and immune competent cells. [The *SCI*® indicates that this paper has been cited in over 360 publications since 1976.]

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In 1972 we began a series of studies to delineate the mechanisms of action of corticosteroids on human lymphoid cells. We determined the precise effect on the circulation versus the functional capabilities of lymphocytes and monocytes[1] as well as neutrophils.[2] My major interest was in the effect of corticosteroids on immune competent cells. My colleague, David C. Dale, was doing work on the effects of corticosteroids on neutrophils.[2] In order to map out the precise kinetics of the effects of steroids on both these cell types, we administered boluses of corticosteroids and followed the distribution of cells by radiolabeling techniques over a period of two to three days. Since we had no idea what the pattern of the kinetics would be, we drew blood quite frequently, often on an hourly to two-hourly basis around the clock. Dale and I would rotate coming in to the NIH Clinical Center in the middle of the night to draw samples from the patients and normal volunteers.

We showed clearly that a major effect of corticosteroids on human lymphocytes was a redistribution of T cells out of the circulation into other body compartments such as the bone marrow.[3] We further went on to delineate the differences between daily and alternate-day corticosteroid regimens on mononuclear cell and neutrophil circulation as well as (together with James E. Balow) on the precise functional capabilities of these cells.[4] These studies were of enormous importance to us later on in our ability to design rational corticosteroid therapeutic regimens, particularly the conversion from daily to alternate-day drug[5] based on the differences of effects of these two regimens on immunological function.

We feel that this paper has been so highly cited because it provides in one major review a series of scientific observations on cellular physiology and immunology and combines this with an extrapolation from the basic scientific observation to a rational approach toward the design of therapeutic regimens of corticosteroids.

1. **Fauci A S & Dale D C.** The effect of in vivo hydrocortisone on subpopulations of human lymphocytes. *J. Clin. Invest.* **53**:240-6, 1974. (Cited 320 times.)
2. **Dale D C, Fauci A S, Guerry D & Wolff S M.** Comparison of agents producing a neutrophilic leukocytosis in man: hydrocortisone, prednisone, endotoxin, and etiocholanolone. *J. Clin. Invest.* **56**:808-13, 1975. (Cited 100 times.)
3. **Fauci A S & Dale D C.** The effect of hydrocortisone on the kinetics of normal human lymphocytes. *Blood* **46**:235-43, 1975. (Cited 95 times.)
4. ----------. Alternate-day prednisone therapy and human lymphocyte subpopulations. *J. Clin. Invest.* **55**:22-32, 1975. (Cited 130 times.)
5. **Thorn G W.** Clinical considerations in the use of corticosteroids. *N. Engl. J. Med.* **274**:775-81, 1966. (Cited 55 times.)

