ALTERNATE-DAY STEROID REGIMEN IN THE TREATMENT OF OCULAR DISEASE*†

BY

SIGMUND SCHUTZ, ROBERT NEWHOUSE, AND JOSEPH DELLO RUSSO

From the Department of Ophthalmology, New York Polyclinic Hospital, New York City

THE systemic use of cortisol and its derivatives has proved invaluable in the management of certain ocular diseases. However, the prolonged use of steroids, so often necessary in the treatment of such conditions as chronic uveitis, frequently leads to serious complications. The incidence of side-effects and their undesirable sequelae varies from case to case, but they are mainly related to the dosage and duration of therapy.

The hazards range from signs of Cushing facies to major life-threatening catastrophes, such as overwhelming infections, gastrointestinal ulceration, and acute adrenal insufficiency. As the ophthalmologist is not usually in a position to control his patient's overall medical status, measures to increase the safety of long-term steroid administration are extremely advantageous.

Harter, Reddy, and Thorn (1963) published the results of studies using a new approach to prolonged oral administration of steroids. Reasoning that the therapeutic (anti-inflammatory) effects of steroids appeared to persist longer than their metabolic effects, it seemed plausible that the use of an intermittent large dosage schedule might avoid the cumulative undesirable metabolic effects of the hormones, and yet be sufficient to maintain the anti-inflammatory properties. The authors selected 58 medical patients with systemic diseases of various types, all of whom required prolonged steroid therapy. Each patient was given the total quantity of steroid required for a 2-day period as a single dose every 48 hours. For example, a patient requiring 10 mg. prednisone four times a day was given 80 mg. before breakfast on alternate mornings. This type of alternate-day dosage proved to be approximately equal in effectiveness, in the opinion of the authors, to the conventional four-times-a-day therapy, and there was a markedly reduced incidence of side effects. Furthermore, it was shown that, using the Thorn test and 17-ketosteroid determinations, there was little of the adrenal suppression that is usually produced by long-term use of steroids.

Materials and Methods

The present study was undertaken in order to determine whether the alternate-day steroid regimen could be applied effectively to the therapeutic requirements of patients with a variety of ocular diseases that usually call for steroid treatment. Beginning in 1964, every patient encountered by us in the Department of Ophthalmology at New York Polyclinic Hospital and in our combined private practices, who required the oral administration of steroids, was placed on the alternate-day regimen. Typical maintenance dosage of prednisone was 20 mg. orally every other morning before breakfast, in place of 5 mg. twice a day.

* Received for publication May 18, 1967.

† Address for reprints: 150 West 55th Street, New York, N.Y., 10019, U.S.A.

462 SIGMUND SCHUTZ, ROBERT NEWHOUSE, AND JOSEPH DELLO RUSSO

Patients were studied with respect to their response to the anti-inflammatory effect of steroids, and the occurrence of side-effects and complications. In a few instances, when the patients were hospitalized, their adrenal functions were studied at different stages in their treatment.

Results

At the time of the submission of this report, fifteen patients with a variety of severe ocular inflammatory diseases had been on this regimen of alternate-day steroid therapy (Table). For obvious reasons, it is not possible to run control or double-blind studies, and we cannot evaluate this entire subject statistically. We can, however, state that, in our clinical judgment of each case, with only one exception, all our patients responded as favourably to the alternate-day regimen as they might be expected to react to the conventional dosage. The one exception was that of Case 15, who experienced a recrudescence of thyrotoxic exophthalmos a few days after being switched to the alternate-day regimen. This patient had been on daily prednisone for 2 months, and had probably developed a significant degree of adrenal cortical suppression. As a result, she had little endogenous adrenal activity, and the dosage of intermittent prednisone was relatively insufficient.

TABLE
RESULTS IN 15 PATIENTS

No. Patient	Age (yrs)	Sex	Diagnosis	Dosage (mg.)	Duration (wks)	Response	Complications	Comments
1	32	M	Sarcoid uveitis	60	30	Good	None	Normal Thorn test in 3rd month of treatment
2	34	F	Sarcoid uveitis	30-50	44	Good	None	Abrupt cessation twice without difficulty; normal Thorn test after 6 months
3	32	F	Central chorio-retinitis	80	2	Good	None	Normal Thorn test after 6 months
4	33	M	Central chorio-retinitis	40	4	Good	None	Uneventful abrupt cessation 1 week before major chest surgery
5	45	M	Pan-uveitis	20	4	Good	None	
6	62	F	Chorio-retinitis	60	8	Good	None	
7	32	F	Toxoplasmic chorio-retinitis	10	52+	Good	None	Used conjointly with Daraprim; uneventful pregnancy
8	72	F	Acute phakotoxic uveitis	20	2	Good	None	Steroids discontinued at time of cataract surgery
9	48	M	Uveitis and dislocated lens	20	24	Good	None	
10	48	F	Chronic iridocyclitis	40	8	Good	None	
11	34	F	Sarcoid uveitis	20	52	Good	None	Cushing facies from 3 years of continuous steroids disappeared after 1 year of alternate-day regimen
12	33	M	Sympathetic uveitis	20-60	104	Good	Pulmonary TB after 1½ years	Normal Thorn test and uneventful abrupt cessation
13	45	F	Chronic anterior uveitis	30-20	21	Good	None	Probably has sarcoidosis
14	63	F	Acute iridocyclitis	20-10	8	Good	None	
15	53	F	Thyrotropic exophthalmos	40	2	Poor	Severe relapse	Had been on daily prednisone for 2 months (See text)

The only distinctly untoward complication occurred in Case 12. This man was being given alternate-day steroids for control of sympathetic uveitis. A routine chest x ray taken during the 18th month of therapy revealed a pulmonary infiltrate. Several sputa were positive for acid-fast bacilli. Prednisone was discontinued abruptly, and only topical steroids were given. The patient was treated with anti-tubercular drugs for 2 months and tubercular signs disappeared completely. After the initial 10 days of anti-tuberculous treatment, he was again given alternate-day prednisone, which he has continued up to the present time, while under coverage of Isoniazid. Evidently the increased susceptibility of steroid-treated patients to tubercular infection is not ameliorated by this programme.

On the whole we are favourably impressed by the therapeutic effectiveness of this regimen. Several patients have maintained good adrenal cortical function in the face of long-term steroid administration which would ordinarily be expected to suppress endogenous production of cortisol. This was demonstrated both by laboratory methods (the Thorn test) and by the ability of these patients to tolerate abrupt steroid withdrawal. The desirability of avoiding adrenal suppression does not require elaboration here.

Summary

A new regimen for long-term oral dosage of steroids, which had proved itself useful in other branches of medicine, was tested in relation to ocular diseases. The longest period of treatment reported here is 2 years.

Its chief advantage over conventional steroid dosage appears to be the avoidance of adrenal cortical suppression while maintaining the anti-inflammatory effect.

There was generally a very low incidence of steroid-induced side-effects (one patient out of fourteen), but the number of patients receiving treatment was too small to draw any firm conclusions.

The treatment is recommended for any patient with normal adrenal function for whom steroid therapy is indicated, since its effectiveness is as great as conventional dosage and the side effects seem to be reduced.

REFERENCES

- HARTER, J. G., REDDY, W. J., and THORN, G. W. (1963). *New Engl. J. Med.*, **269**, 591.
HARTER, J. G., HALL, A. P., and BAYLES, T. B. (1965). *Arthr. and Rheum.*, **8**, 445.
DI RAIMONDO, V. C., and FORSHAM, P. H. (1956). *Amer. J. Med.*, **21**, 321.
REICHLING, G. H., and KLIGMAN, A. M. (1961). *Arch. Derm.*, **83**, 980.
SOYKA, L. F., and SAXENA, K. M. (1965). *J. Amer. med. Ass.*, **192**, 225.
SIEGEL, S. C., HEIMLICH, E. M., RICHARDS, W., TAYLOR, W. F., and KELLEY, V. C. (1965). *J. Allerg.*, **36**, 209.