Eosinophile Levels in Hospitalized Psychotics During Combined Testosterone-Estrogen Therapy. (18443)

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In previous communications, the possibility that some forms of psychosis are caused by an operative or relative excess‡ of oxycorticosteroid was postulated(1,2) and the results of therapy with massive combined doses of testosterone and estradiol were reported (3,4). These results were improvement in 23 (58%) and the attainment of convalescent status in 12 (30%) in a series of 40 hospitalized psychotics.

As an index of adrenocortical activity, eosinophile levels were followed before and during the course of therapy since 11-oxysteroid secretion is reported to be reflected more sharply and consistently by the change in circulating eosinophiles than by the absolute lymphocyte count(5).

Materials and method. 17 patients chosen

TABLE I. Correlation of Improvement with DEC "Prognostic" Index.

Sex	Age	Diagnosis	Total dosage T/E, mg	Results T/E therapy	DEC index
F	20	S.-c.	1300/43.3	++++	36.7
F	30	S.	1100/36.6	++++	25.0
F	23	S.-s.	800/26.6	++	14.4
M	53	M.D.-d.	1450/76.6	++	13.6
F	56	M.D.-d.	800/26.6	++++	11.0
M	34	S.-p.	1250/41.8	++++	10.2
F	51	M.D.-d. inv.	487/31.6	++++	7.1
F	29	S.-p.	1100/36.6	0	5.9
M	46	S.-p.	1250/41.7	0	5.2
M	62	M.D.-m.	1300/43.3	0	5.1
F	17	S.-p.	750/33.2	(++++)*	3.1
F	30	S.-c.	1125/33.2	+	3.1
M	56	M.D.-m.	1200/36.6	(++)*	2.9
F	34	S.	900/31.6	+	2.7
M	53	I.M.-p.	1150/36.3	0	1.7
F	53	I.M.-p.	750/38.3	0	1.4
F	47	I.M.	1050/61.6	0	0.92

* Transient.
S.—Schizophrenia.
S.-s.—Schizophrenia, simple type.
S.-c.—Schizophrenia, catatonic type.
S.-p.—Schizophrenia, paranoid type.
M.D.-d.—Manic-depressive, depressed.
M.D.-m.—Manic-depressive, manic.
M.D.-d.inv.—Manic-depressive, depressed. involutional.
I.M.—Involutional melancholia.
I.M.-p.—Involutional melancholia, paranoid.
++++ = convalescent status; +, ++, +++ = improvement; 0 = unimproved.
DEC Index—Ratio of peak resting eosinophile level during or after course of treatment to average of resting levels before treatment.
Compiled in part from Data *in press*, Sackler *et al.* Sex Steroid Therapy in Psychiatric Disorders. Part I: Clinical Findings. *Acta Psych. et Neurol.*

* Deceased.

‡ By operative or relative excess is meant that relative concentration that produces an effect as distinguished from the absolute concentration.

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at random from a series of 40 were subjected to weekly eosinophile determinations before, during and after a course of combined sex steroid therapy. The basic treatment procedure consisted of administration of 50 to 100 mg of testosterone propionate and 1.67 to 3.33 mg of estradiol benzoate in a single intragluteal injection administered daily for a period of 4 weeks. Fasting blood was obtained by finger puncture and direct counts were promptly performed according to the method described by Thorn(6), employing the Levy 0.2 mm deep chamber and eosin-acetone diluting fluid. The average of 4 chamber counts was computed for each determination (Table I).

Results. 1. The pre-treatment eosinophile levels fluctuated erratically during the several weeks they were followed.

2. The eosinophile counts of all but 3 patients rose sharply during the course of testosterone-estrogen therapy, as may be seen in Fig. 1. Reaching a peak usually in the latter 2 weeks of the 4-week period of treatments, they increased as much as 30-fold before reverting to lower levels 4 to 5 weeks after therapy.

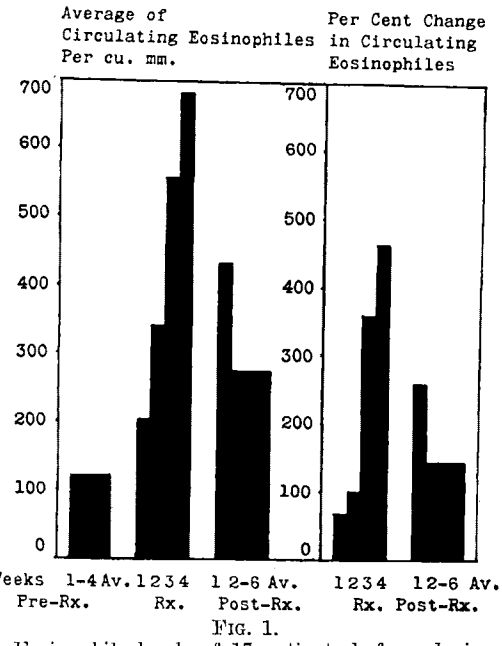

FIG. 1.
Eosinophile levels of 17 patients before, during, and after testosterone-estrogen therapy.

3. There was positive correlation between improvement in the patients' clinical status and the attainment of higher eosinophile levels, as demonstrated in Fig. 2.

Discussion. In our recent report on "Some Common Physiologic Denominators of Histamine, Sex Steroids, Insulin and Electroconvulsive Therapies"(7), the effect of these agents on adrenocortical activity was presented. It was considered diphasic—stimulation initially (by all but sex steroids), and then depression (by all these therapies, including sex steroid). In many of the histamine treated patients we have noted a slow but steady rise in the eosinophile level. Courses of insulin coma and electroconvulsive therapies have also been reported(8-11) to be associated with a rise in eosinophile or lymphocyte resting level.

Finn Rud(7) considers a rise in the eosinophile count a favorable prognostic sign in psychosis: "In many cases a close relationship to the clinical course was shown, the eosinophile count increasing during improvement of the psychic condition." Rud also followed the eosinophile levels of psychotic patients during insulin shock therapy. While he found a characteristic *decrease* during the first few hours after injection of each dose of insulin, during extended treatment there was a distinct *increase* in the resting level of eosinophiles, often of several hundred per-cent. This increase first appeared in the second or third week and gradually reverted to the original level after the conclusion of

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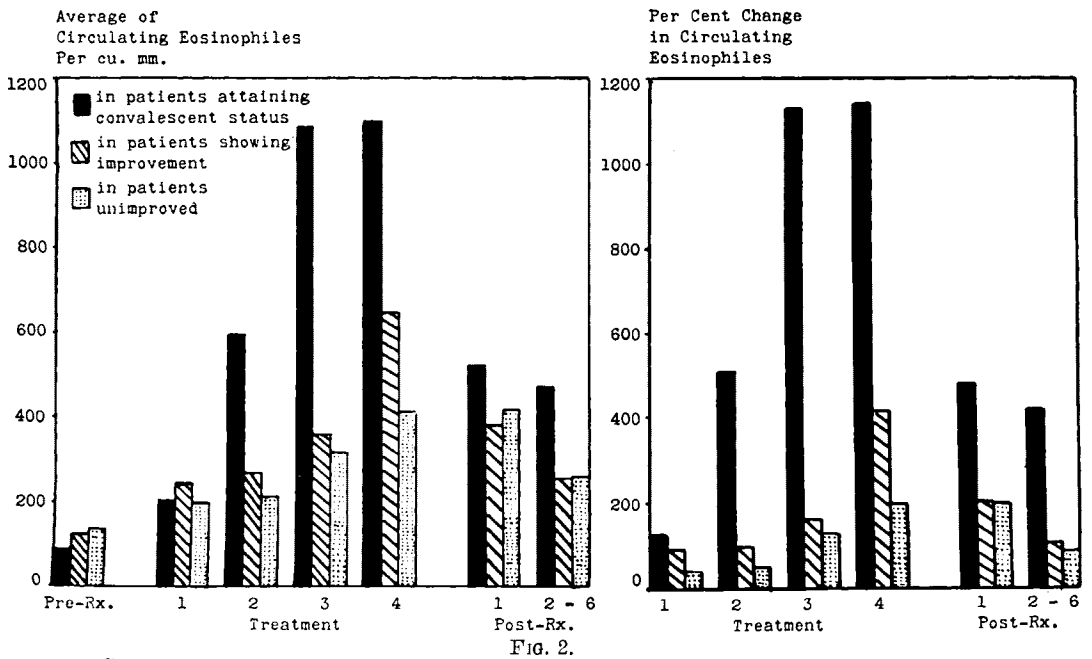

FIG. 2.

Correlation between clinical improvement and change in circulating eosinophile levels of 17 patients: 6 attained convalescent status, 5 improved, and 6 unimproved.

therapy. This may be interpreted as representing a "washing out" of adrenocortical hormone during the acute stress of shock treatment, with eventual attainment of lower basal levels of secretion of 11-oxysteroids as reflected in the higher eosinophile counts.

There is evidence that the sex steroids may have a direct antagonistic effect on corticosteroids. Venning and Brown(12), Talbot *et al.*(13) and Albright(14) have each reported a marked fall in 11-oxycorticosteroid excretion in patients following the administration of testosterone propionate. The latter also reports that Dr. Edward Dempsey has found decreased steroids in the cortices of rats as well as in biopsies from humans following testosterone administration. The eosinophile changes here reported tend to support their observations.

Summary and conclusions. 1. The direct eosinophile counts of the majority of a group of 17 psychotic patients rose sharply during the course of massive combined testosterone-estrogen therapy. 2. There was an apparent positive correlation between improvement in the patients' clinical status and the degree of eosinophilia attained. 3. An anti-adrenocortical effect at least in relation to blood eosinophile levels of sex steroids is suggested.

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