

# RATIONALE AND EFFICACY OF DAILY SINGLE DOSE CORTICOID THERAPY IN CERTAIN CASES OF OVULATORY FAILURE AND HIRSUTISM

## A Preliminary Report\*

by

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It is well known that adrenal cortical dysfunction may contribute to certain types of ovulatory failure and hirsutism. Glucocorticoid therapy has been found beneficial in such conditions, and this probably acts by suppressing the secretion of abnormal adrenal steroids, which is under the control of ACTH stimulation. It is pertinent to mention that glucocorticoid administration has also been shown to increase gonadotropin secretion from the pituitary in normal individuals. This may be brought about by suppressing the secretion of adrenal sex steroids thereby relieving the pituitary-gonadal axis from inhibition, and/or by acting directly on the hypothalamic-hypophyseal axis. Hithertofore, glucocorticoid has been given every 6 or 8 hours for effective suppression of adrenal cortical function, and thus the total daily dosage has been relatively high.

In individuals who remain active

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during the day and sleep at night, ACTH in large quantities is secreted from the pituitary in the early morning hours, while during the rest of the day ACTH secretion remains at low ebb because of the circadian rhythmic activity of the hypothalamus. As a result, secretion of about 70 per cent of total output of adrenal cortical hormones occurs during 8 hours in the morning, whereas the remaining 30 per cent is secreted throughout the rest of the day. Recently, it has been shown in short-term experiments that daily administration of a single dose of glucocorticoid at midnight to such individuals effectively suppresses the adrenal cortical secretion, presumably by inhibiting the surge of ACTH secretion in the early morning hours.

In view of the above observations, it has been thought worthwhile to study the effect of such daily single dose corticoid therapy on certain types of ovulatory failure and hirsutism, and to elucidate the effect of long-term treatment on the adrenal cortical function.

### Material and Methods

Twenty women with various disorders have been treated with glucocorticoids, and this preliminary

report is based on the observations made in 17 of them who have had some follow up. Ten of these women had Stein-Leventhal syndrome, two had secondary amenorrhoea, two had primary amenorrhoea, two had idiopathic hirsutism and the remaining one had hyperthecosis of the ovary. Dexamethasone in dosage of 0.5 and 1 mg. has been administered once daily at about midnight. Other dosage schedules have also been tried in some of these patients. One patient has been treated only with prednisolone, and another has received prednisolone prior to the institution of dexamethasone therapy. The details are given in Table I.

A careful history has been taken in each case with special reference to their previous menstrual status, and the basal body temperature (BBT) record has been maintained for at least four months prior to institution of corticoid therapy. During treatment BBT chart has been maintained and the presence or absence of menstrual molimina recorded. No endometrial or detailed hormonal studies have yet been carried out.

#### *Results and Comments*

The results are summarized in table I. Of the ten patients with Stein-Liventhal syndrome, six have experienced one or more probable ovulations during corticoid therapy. During a total period of about 32 months of use of corticoid in these patients there are evidences of at least 16 ovulations. One patient in this group has been taking prednisolone and she has conceived. Although she has received pred-

nisolone twice daily, the main dosage has been given near about the midnight with the idea of suppressing the surge of ACTH secretion in the early morning hours. In the remaining four patients with S.L. syndrome, there has been no response during a total period of about 11 months of corticoid therapy.

Of the four patients with primary and secondary amenorrhoeas, only one with secondary amenorrhoea has experienced three ovulatory periods during three months of corticoid therapy. The remaining three have not responded during a total period of 9 months of corticoid administration.

The patient with hyperthecosis has had two probable ovulations, one of these was not followed by menstruation.

In one patient with idiopathic hirsutism and infrequent ovulation, the ovulation has become more regular and she has conceived during corticoid administration.

The other patient with idiopathic hirsutism, who has been experiencing regular ovulatory periods, has received 0.5 mg. of dexamethasone once daily at about midnight over a period of 20 months. Urinary 17-ketosteroids (17-KS) have been estimated before and during corticoid therapy at some intervals. Her hirsutism has decreased and the urinary 17-KS have been kept suppressed during the period of corticoid administration. The average excretion of urinary 17-KS per 24 hours has been 14.8 mg. prior to corticoid therapy, and the average of 13 determinations during corticoid treat-



TABLE I  
Details of women on corticoid therapy

S. No.	Name & Age	Diagnosis	Corticoid and dosage	Duration of therapy	Results	Remarks
1	S. (22)	S.L. Syndrome	Dexamethasone 1 mg. once daily at about midnight.	Two months	Two ovulatory periods.	....
2	A.P. (33)	"	Dexamethasone 0.5 mg. once daily at about midnight.	Three months	No response	Previous wedge re-section of ovaries did not give sustained benefit.
3	A.S. (20)	"	"	Four months	One ovulatory period.	....
4	G.D. (28)	"	"	Six months	Three ovulatory periods.	Previous wedge re-section of ovaries was followed by 3 ovulatory periods; then she developed amenorrhoea.
5	S.J. (21)	"	"	Six months	Five ovulatory periods.	....
6	S.J. (29)	"	(a) Dexamethasone 1 mg. once daily at about midnight. (b) Dexamethasone 0.5 mg. once daily for first 15 days each month. (c) Dexamethasone 0.5 mg. twice daily for first 15 days each month.	Three months Three cycles Three cycles	Three ovulations but two periods. No response No response	Has gained weight and developed purple striae. .... ....
7	K.D. (30)	"	Dexamethasone 0.5 once mg. daily at about midnight.	Three months	No response	....
8	S.M. (32)	"	"	Three months	No response	....
9	K.N. (28)	"	Dexamethasone 0.5 once mg. daily at about midnight.	Six weeks	No response	Has gained weight and discontinued medication.
10	J.B. (21)	"	(a) Prednisolone 10 mg. daily in divided doses. (b) Prednisolone 5 mg. at 11 P.M. and 2.5 mg. at 8 A.M. daily.	Two months Three months	Ovulatory period once. Irregular rises in BBT; has become pregnant at the end of 3 months.	.... ....

11	K. (26)	Primary amenorrhea.	Dexamethasone 0.5 mg. once daily at about midnight.	Three months	No response	....
12	M.V. (25)	"	"	Three months	No response	....
13	S. (28)	Secondary amenorrhea.	"	Three months	No response	....
14	S.B. (29)	"	"	Three months	Three ovulatory periods.	....
15	P.K. (19)	Hyperthecosis of ovary.	Dexamethasone 1 mg. once daily at about midnight.	Three months	Two ovulations but only one period.	....
16	A.S. (26)	Idiopathic hirsutism with irregular ovulations.	(a) Prednisolone 5 mg. at 11 P.M. and 2.5 mg. at 8 A.M. daily. (b) Dexamethasone 0.5 mg. once daily at 11 P.M.	Three months	Two voluntary periods.	....
17	S.J. (20)	Idiopathic hirsutism with regular ovulatory menses.	Dexamethasone 0.5 m.g. once daily at about midnight.	Three months	Two ovulations; has become pregnant during the second ovulation.	....
				Twenty months	Hirsutism has decreased; urinary 17-KS has been kept suppressed throughout the period of treatment.	....

ment has been 5.2 mg. per 24 hours. These findings indicate that with continued exposure of the hypothalamic-hypophyseal axis to higher level of glucocorticoid at or after midnight, when normally the circulating glucocorticoid is at its lowest level, does not alter the timing of circadian rhythm so as to cause an escape from corticoid suppression.

### Conclusions

Although the number of women studied is too small to warrant any definitive conclusion, the results indicate that daily single dose corticoid therapy is effective in suppressing adrenal cortical function on a long-term basis. Such therapy may be beneficial in certain groups of patients with ovulatory failure and hirsutism. Work is in progress for further elucidation of the problem.

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