

Appendix 3

Report of the Task Force on Metabolic Effects

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Pituitary-Ovarian Function

The controversy as to whether oral contraceptives inhibit at the pituitary or at the ovarian level appears now to be resolved. Diczfalusy (1965) and his group present convincing evidence that these compounds inhibit at the pituitary level and that they interfere predominantly with the synthesis and/or release of LH rather than FSH. Similar results have been obtained by Lin (1964), Martin (1961), Taymor (1964 and 1965), and Ryan et al. (1966). The differences in these results and those obtained by Loraine and others are probably related to differences in methodology. Diczfalusy's group employed technics for estimation of LH and FSH individually whereas Loraine's conclusions that progestational compounds inhibit ovulation without affecting HPG excretion were based on a method for determination of total gonadotrophic activity. Furthermore, in Diczfalusy's study, oral contraceptive steroid combinations were administered simultaneously with courses of HMG or HHG followed by HGG. Results showed that administration of these compounds in dosages three times higher than those used for ovulation inhibition did not interfere with the ovarian reaction to exogenous gonadotrophins.

Available evidence indicates that resumption of ovulation after cessation of oral contraceptives is prompt, occurring in 4 to 8 weeks in most cases. In a few women, amenorrhea persists for 6 months or more. This is not unlike the occasional protracted anovulation following pregnancy or lactation. Fertility is the best indicator of adequate pituitary-ovarian function. Goldzieher (1962) reported 62 percent success in the first cycle in women discontinuing medication with intent of becoming pregnant, which compares favorably with the 34 percent conception in the first cycle after stopping mechanical or chemical contraceptives noted by Tietze (1959). Pincus (1964) found a pregnancy rate of 233 per 100 years of exposure

after oral contraceptives were discontinued as compared with a rate of 17 before use in the same women. Pregnancy outcome was satisfactory with no significant increase in abortion, prematurity, abnormality, or developmental anomaly—Pincus (1964), Rice-Wray (1965).

Long-term effect (beyond 6 to 8 years) of oral contraceptives on the pituitary-ovarian interrelation, on normality and duration of ovarian function, and on fertility throughout the reproductive span is not known. Answers will require long-term physiological study and complex statistical control.

Pituitary-Adrenal Function

Oral contraceptives have been observed to produce increased cortisol-binding by serum proteins but urinary excretion data for 17 hyroxysteroids and 17 ketosteroids have been equivocal. Recent work seems to clarify the effect on pituitary-adrenal function. ACTH activity was studied during progestin treatment by Leach and Margulis

Table 1.—Comparison of ACTH response during and after therapy

Patient	During therapy		After therapy		Difference (mg.)	
	Control	ACTH	Control	ACTH	Before	After
E. J.-----	4.6	19.6	9.3	27.3	15.1	18.0
H. L.-----	5.9	9.1	4.4	14.5	3.2	10.1
A. D.-----	3.6	5.7	5.3	14.4	2.1	9.1
G. E.-----	2.0	8.6	8.8	28.6	6.6	19.8
H. L.-----	6.4	10.1	6.0	14.0	3.7	8.0
P. S.-----	5.9	9.3	7.5	23.0	3.4	15.5
J. W.-----	3.7	11.6	7.0	18.4	7.9	11.4
A. B.-----	8.1	10.2	6.1	31.4	2.1	25.3
C. H.-----	1.1	9.6	13.6	17.1	8.5	3.5
G. R.-----	3.0	17.5	7.7	19.7	14.5	12.0
A. K.-----	3.6	6.5	12.8	16.3	2.9	3.5
N. H.-----	2.6	10.5	5.6	17.9	7.9	12.3
Mean-----	4.2	10.69	7.8	20.2	6.4	12.38

From Leach and Margulis.