# PAPERS AND ORIGINALS

## Oral Contraceptives, Depression, and Libido

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### Summary

Depression, headaches, and libido were rated in 272 women before starting a contraceptive method and at intervals during the first year of use—54 were fitted with an intrauterine device (I.U.D.) and 218 used one of three oral contraceptives. Side effects caused 25% of the oral contraceptive group and 13% of the I.U.D. group to stop the method. Depression, headaches, and loss of libido were the most common reasons for stopping oral contraceptives and breakthrough bleeding was the most common reason for stopping the I.U.D.

The group of women who stopped or changed their oral contraceptives during the survey were compared with the group who remained on the same oral contraceptive throughout. The former had higher mean depression and neuroticism scores at the first clinic visit and contained more women with a history of premenstrual weepiness, depression during pregnancy, outpatient psychiatric treatment, and treatment with antidepressants. Changes in the depression, headache, and libido ratings throughout the survey are presented.

## Introduction

The incidence of severe depression among women using oral contraceptives is about 5-6%, compared with 1-2% in women using other methods of contraception (Lewis and Hoghughi, 1969; Herzberg and Coppen, 1970; Herzberg et al., 1970).

There is evidence that women with a history of depression are more likely to develop psychiatric side effects from oral contraceptives. Kaye (1963) reported the cases of three women with severe depression while taking oral contraceptives, two of whom had been under psychiatric care previously. Nilsson et al. (1967) found that women with psychiatric symptoms while taking Anovlar were frequently those who had had medication for psychiatric illness or emotional disturbances during early pregnancy, and Lewis and Hoghughi (1969) also found that women who were depressed while taking oral contraceptives were likely to be those with a history of depression.

In 1968 a prospective study was started to investigate the association between oral contraceptives and changes in mood and libido. In the present paper the incidence of symptoms in women taking oral contraceptives is compared with that in women fitted with an intrauterine device (I.U.D.). Differences between those women who found oral contraceptives satisfactory during the first year and those who experienced adverse effects and stopped or changed their oral contraceptive are also presented.

Further results from the prospective survey will give a full analysis of the individual items of the depression questionnaire.

## Methods

The 272 women who participated in the survey attended F.P.A. clinics and were either starting to use oral contraceptives or were being fitted with an I.U.D. All the women had been married for at least six months and had neither given birth nor used oral contraceptives during the previous year; they were between 20 and 45 years of age. Data were collected from the subjects at five consecutive clinic visits.

At the first visit, before using the contraceptive, baseline data were obtained by a standardized questionnaire completed by the interviewing doctor; depression, libido, and personality were assessed by self-rating questionnaires described below. One of three oral contraceptives (Gynovlar, Lyndiol 2.5,\* or Norinyl-1) was prescribed or an I.U.D. was fitted. Subsequent visits occurred at intervals of 2, 5, 8, and 11 months from the

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<sup>\*</sup>The survey began 18 months before the recommendations of the Committee on Safety of Drugs (1970) were circulated.

initial visit, when further standardized data were obtained and the self-rating questionnaires were again completed. For all subjects the clinic data were supplemented by depression ratings obtained by postal follow-up and by further information supplied by their general practitioners.

The baseline data consisted of personal measurements (age, height, and weight), family data (date of marriage, husband's age, number of children and their age range), obstetric histories (number of stillbirths, miscarriages), and the presence and duration of depression during pregnancy and postpartum. Further details of the regularity and lengths of menstrual cycles, the incidence and severity of headaches, the age of menarche, and premenstrual symptoms were recorded. All women were asked whether they wished to increase the size of their families at some time. Personal histories of the subjects were noted (birth weight, illness during the first year of life) together with histories of either outpatient or inpatient psychiatric treatment and use of psychotropic drugs and anticonvulsants. Finally, any history of family mental illness and death or separation of parents were noted.

At every subsequent visit the structured questionnaire asked the day of the menstrual cycle, the contraceptive being used, and the number of cycles of use. Any breakthrough bleeding, amenorrhoea, and headaches were recorded, and weights were measured. If the subject had stopped the contraceptive since the last visit a separate questionnaire was completed giving the reasons.

Throughout the survey three questionnaires were used to estimate depression, libido, and personality respectively:

Depression Scale.—This scale for measuring depression was the same as that described in our previous study where its use as a monitor of premenstrual depression was validated (Herzberg et al., 1970). It is a modification of the Beck inventory (Beck et al., 1961).

Libido Scale.—Three aspects of sexual behaviour were assessed by separate self-rating scales. These were sexual interest, frequency of intercourse, and sexual satisfaction. The full scale is given in the Appendix.

Personality.—A shortened version of the Eysenck Personality Inventory for measuring extraversion and neuroticism was used (Eysenck and Eysenck, 1964).

## Results

The sizes and distribution of age, social class, and parity in the four contraceptive groups are shown in Table I. Nearly one-half of the women were given Norinyl-1 initially and the remainder were divided almost equally between the other three contraceptives. The groups do not have significantly different age or social class distributions but the numbers of children reflect the practice of fitting the I.U.D. only in parous women. There were no significant differences between the different oral contraceptive preparations, and the 272 women were divided into three main groups (Table II)—those who remained on the same contraceptive throughout, those who stopped or changed within the one-year period, and those who failed to attend the follow-up clinics and did not return the postal questionnaire.

The high proportion of women who either stopped or changed their oral contraceptive is surprising—44% of women using oral contraceptives stopped or changed the method during the first year, 37% remained on the same oral contraceptive (Table II); by contrast, only 13% of women on the I.U.D. changed their method of contraception. The proportions in each group for whom information was not complete were about equal.

The composition of the group that stopped or changed oral

TABLE I-Distribution of Age, Social Class, and Parity in the Four Contraceptive Groups

			I.U.D.	Gynovlar*	Lyndiol 2.5*	Norinyl-1*
Mean age ±	S.E. o	f mean	31·31 ± 0·78	29·43 ± 0·92	29·92 ± 0·79	29·86 ± 0·49
Age: <24 25-29 30-34 35-39 >40			3 (6) 15 (29) 22 (42) 10 (19) 2 (4)	9 (24) 10 (27) 11 (30) 5 (14) 2 (5)	13 (25) 10 (20) 18 (35) 6 (12) 4 (8)	22 (17) 47 (36) 30 (23) 22 (17) 9 (7)
,	Total†		52	37	51	130
Social class: I, II III IV, V	·		16 (30) 29 (55) 8 (15)	7 (20) 24 (69) 4 (11)	19 (38) 28 (56) 3 (6)	34 (27) 77 (60) 15 (13)
-	Total§		53	35	50	126
Parity: 0 1 2 >3	• •		0 (0) 7 (13) 28 (52) 19 (35)	7 (19) 7 (19) 23 (62) 0 (0)	16 (31) 9 (18) 16 (31) 10 (20)	26 (20) 22 (17) 54 (42) 28 (21)
-	Total		54	37	51	130

Percentages in parentheses.
\*Gynovlar (norethisterone acetate 3 mg and ethinyloestradiol 0·05 mg). Lyndiol 2·5 (lynoestrenol 2·5 mg and mestranol 0·075 mg). Norinyl-1 (norethisterone 1 mg and mestranol 0·05 mg).
†Two women in the I.U.D. group did not give their ages.
‡General Register Office (1966).
\$Eight women did not give their husband's occupation.

TABLE II-Composition of the Survey. Numbers of Women in Each Category

Contraceptive	Using Same Contraceptive Throughout	Stopping or Changing Contraceptive	Not Known	Total
Gynovlar	12 (32·4)	16 (43·2)	9 (24·3)	37
Lyndiol 2·5	14 (27·5)	26 (51·0)	11 (21·6)	51
Norinyl-1	54 (41·5)	54 (41·5)	22 (17·0)	130
Total oral contraceptives I.U.D	80 (36·7)	96 (44·0)	42 (19·3)	218
	40 (74·1)	7 (13·0)	7 (13·0)	54
Total	120 (44·1)	103 (37-9)	49 (18·0)	272

Figures in parentheses are percentages of the figures in the right-hand column.

TABLE III—Composition of the "Stop/Change" Group

0-10	Change to Another Oral	Stop Oral Contraceptives because of:		Total	
Oral Contraceptive	Contraceptive	Side Effects	Wanting a Pregnancy	Total	
Gynovlar Lyndiol 2·5 Norinyl-1	3 (18·8) 10 (38·5) 18 (33·3)	11 (68·8) 12 (46·2) 32 (59·3)	2 (12·5) 4 (15·4) 4 (7·4)	16 26 54	
Total	31 (32·3)	55 (57·3)	10 (10-4)	96	

Figures in parentheses are percentages of figures in the right-hand column.

TABLE IV-Reasons Given for Stopping the Contraceptive Method

Stated Reason	I.U.D.	Lyndiol 2·5	Norinyl-1	Gynovlar	% of Women with Side Effect in Oral Contraceptive Stop/Change Group (No. = 86)*
Weight gain	6	3 1 6 6 5 2 1 7	4 3 5 15 13 7 4 3 20	1 1 4 5 5 1 1 5	9·3 4·7 8·1 29·1 27·9 19·8 8·1 5·8 37·2

<sup>\*</sup>All women who stopped oral contraceptives because they wanted a pregnancy are excluded.

contraceptives is given in Table III, which shows there were only minor differences between the three brands of oral contraceptives, and that 57% of women in this group discontinued oral contraceptives because of side effects. It can be concluded that at least 25% of women (55 out of 218) who started oral contraceptives have decided within one year that they do not like the method.

The reasons given for stopping the contraceptive method are given in Table IV (10 women who stopped using oral contraceptives because they wanted a pregnancy were excluded). The I.U.D. was removed from seven women—six because of breakthrough bleeding and one for no specified reason. Headaches, depression, and loss of libido were the most common reasons stated for stopping oral contraceptives.

In the following sections we describe the variations in depression, libido, headaches, and weight that occurred throughout the survey. Two sets of comparisons are made: (a) between the women who retained the I.U.D. (I.U.D. group) and the total oral contraceptive group (O.C. total), (b) between the I.U.D. group, those women who remained on the same oral contraceptive for one year (O.C. throughout), and those women who stopped or changed oral contraceptives within one year (O.C. stop/change).

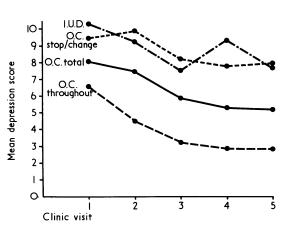


FIG. 1—Mean depression scores at each clinic visit. A decrease in depression score reflects a decrease in depression.

#### DEPRESSION

The mean depression scores from the Beck Inventory for each visit are shown in Fig. 1. Regressions of these mean scores on clinic visit were obtained for the O.C. total and I.U.D. groups, and were compared by analysis of covariance. The regression line for the O.C. total group was significantly lower than that for the I.U.D. group. A similar analysis comparing the O.C. throughout, O.C. stop/change, and I.U.D. groups showed that the regression line for the O.C. throughout group was significantly lower than for the other two. These results were substantiated by a sophisticated regression analysis which allowed for the change of the depression score over the menstrual cycle reported previously (Herzberg et al., 1970). These results will be reported in a further publication.

We conclude that the I.U.D. group was significantly more depressed than the O.C. total group both initially and throughout the survey. Also the O.C. throughout group was significantly less depressed than the O.C. stop/change and the I.U.D. groups.

The numbers of women in each group whose scores increased or decreased between visit 1 and the other visits were compared

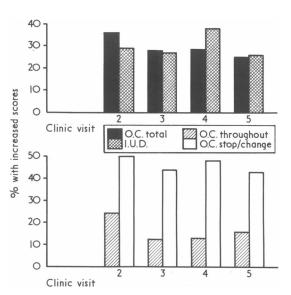


FIG. 2—Percentages of women in each group that increase their depression scores from visit one.

using  $\chi^2$ . Fig. 2 shows the percentages of women in each group whose depression scores increased from visit 1; there were no significant differences between the O.C. total and I.U.D. groups. The proportion of women in the O.C. stop/change group having increased scores was significantly greater (P < 0.01) on each occasion than the proportion in the O.C. throughout group.

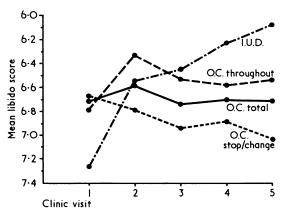


FIG. 3—Mean libido scores at each clinic visit. A decrease in libido score reflects an increase in libido.

In an attempt to identify depressive effects of oral contraceptives in a non-depressed population the O.C. total group was subdivided into women who were initially "depressed" or "non-depressed," using a dividing score of 9, which corresponded to the mean depression score at visit one. The results are shown in Table V. There were no differences between the O.C. total and I.U.D. groups, but significantly more of the women in the O.C. stop/change group who were initially non-depressed became depressed; significantly more of the women in the O.C. stop/change group who were initially depressed remained depressed.

#### LIBIDO

The libido scores from the three separate scales were summed to give an overall measure of libido. The mean libido scores for each group and at each clinic visit are shown in Fig. 3. Regression lines of the mean libido scores on clinic visit for the O.C. total and I.U.D. groups were compared by analysis of covariance. There was a significant difference in slope, indicating that the I.U.D. group had a continual increase in sexual interest, frequency of intercourse, and experienced greater satisfaction, whereas the O.C. total group showed little change. For the O.C. stop/change group libido decreased from the first to the last visit, and for the O.C. throughout group libido initially increased but did not show the progressive improvement of the I.U.D. group.

#### **HEADACHES**

The percentages of women in each group who complained of moderate or severe headaches at each clinic visit are shown in Fig. 4. There was an increase in the incidence of such headaches

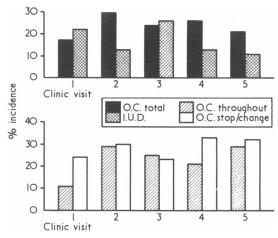


FIG. 4—Percentage incidence of moderate or severe head-aches within each group at each clinic visit.

TABLE V-Changes in Depression Scores in Women who were Initially Depressed and those Initially Not Depressed

Graun			Visit 2		Visit 3		Visit 4		Visit 5	
Group			Not Depressed	Depressed	Not Depressed	Depressed	Not Depressed	Depressed	Not Depressed	Depressed
					Initially De	pressed				
I.U.D O.C. throughout O.C. stop/change	::	::	8 11 10	11 8 27	8 16 9	11 5 23	11 16 14	8 2 18	9 16 11	6 3 16
Total	••	••	29	46	33	39	41	28	36	25
χ² and significance			5·13, N.S.		11·84, P<0·01		9·83, P<0·01		8·83, P<0·05	
					Initially Not 1	Depressed	<u> </u>			
I.U.D O.C. throughout O.C. stop/change	::	::	19 56 46	2 2 11	18 60 54	3 0 3	18 59 48	3 1 4	20 59 32	1 1 6
Total		٠	121	15	132	6	125	8	111	8
χ² and significance	7·31, P < 0·05							·		

Footnote: All  $\chi^2$  tests with O.C. throughout and O.C. stop/change combined in the above tables are not significant.

TABLE VI-Mean Weight at Each Visit (kg)

	Visit 1	Visit 2	Visit 3	Visit 4	Visit 5
O.C. throughout O.C. stop/change O.C. total I.U.D	58·66	59·26	59-66	59·47	59·19*
	58·80	58·75	57-66‡	58·21°	56·91†
	58·74	58·99*	58-68*	58·88°	58·33‡
	61·66	62·30	62-44	62·66	64·04

<sup>\*†‡</sup>Significance of difference from I.U.D. group <0.05, <0.02, <0.01 respectively.

in the O.C. total group after visit 1, which was also apparent in both the O.C. throughout and the O.C. stop/change groups. We conclude that oral contraceptives caused headaches but that some women were prepared to tolerate these side effects and continued using oral contraceptives.

#### WEIGHT

The mean weights of each group for each clinic visit are shown in Table VI. There were significant differences between the mean weights of the O.C. total and I.U.D. groups after visit 1; other significant differences are indicated. An analysis of covariance on regression lines fitted to the means shown in Table VI indicated that there was a significant upward trend in the I.U.D. group but that there were no significant trends in the other groups.

#### PREDISPOSING FACTORS

The previous sections described differences in depression, libido, and headaches. The data obtained at visit 1 for the I.U.D., O.C. throughout, and O.C. stop/change groups were analysed to identify factors predisposing to these symptoms. The only significant differences (P < 0.01) were between the O.C. throughout and O.C. stop/change groups. These indicated that the O.C. stop/change group had higher incidences of premenstrual weepiness and outpatient psychiatric treatment, had more severe and longer depression during pregnancy, and used antidepressants more frequently. By contrast there were no differences in either the severity or duration of post-partum depression.

The mean depression scores at the first visit for three subgroups of the O.C. stop change group, which consisted of those women who changed because of headaches, depression, or loss of libido, were compared with the remaining women in this group whose reasons for stopping or changing were known. The resulting means are shown in Table VII. Those who changed because of headaches did not have a baseline depression score significantly different from those who changed for other reasons. Those who changed because of depression or loss of libido had a mean depression score which was almost twice the mean score of the remainder.

There were no differences between the I.U.D., O.C. throughout, and O.C. stop change groups for age; age of menarche; length of the menstrual cycle; premenstrual symptoms other than weepiness; parental separations, divorce, or death; birth weight; feeding problems or serious illness during first year of life; or use of tranquillizers, sedatives, or night sedation.

TABLE VII—Subgroups that Change for a Specific Reason, Baselinc Depression Scores

	No.	Mean ± S.E. of Mean and Significance of Difference
Change/depression Remainder	25 44	$\begin{array}{c} 11.04 \ \pm \ 1.46 \\ 6.80 \ \pm \ 0.85 \end{array} \left\{ \begin{array}{c} P < 0.02 \end{array} \right.$
Change/headaches Remainder	28 41	$\begin{array}{c} 8.54 \ \pm \ 1.35 \\ 8.20 \ \pm \ 0.97 \end{array} \bigg\{ \ \text{N.S.}$
Change/loss of libido Remainder	20 49	$\begin{array}{c} 12.65 \pm 1.68 \\ 6.57 \pm 0.75 \end{array} \left\{ \begin{array}{c} P < 0.001 \end{array} \right.$

The mean neuroticism and extraversion scores obtained from the short version of the Eysenck Personality Inventory are shown in Table VIII. There were no differences between the mean extraversion scores, but the O.C. stop/change and the I.U.D. groups had mean neuroticism scores significantly higher than that for the O.C. throughout group.

TABLE VIII—Neuroticism and Extraversion Scores (Mean ± S.E. of Mean)

	Neuroticism	Extraversion
O.C. throughout O.C. stop/change O.C. total	 $\begin{array}{cccccccccccccccccccccccccccccccccccc$	3·89 ± 0·18 3·81 ± 0·16 3·85 ± 0·12 4·00 ± 0·25

<sup>\*</sup>Significantly different from O.C. throughout at P = 0.01.

## Discussion

In this survey the incidence of changes in women taking oral contraceptives has been compared with that found in a group using the I.U.D. The two methods of contraception are comparable since the I.U.D. provides reversible contraception almost as effective as oral contraceptives (Mills, 1970) and contraception is removed from the act of intercourse. Further, the introduction of an I.U.D. provides a definite point from which changes can be dated.

The initial mean depression score of the I.U.D. group was higher than the O.C. total group. This preselection bias may result partly from the well-publicized association between depression and oral contraceptives. The mean depression scores of the O.C. throughout and the I.U.D. groups decreased from the first visit, indicating an improvement of mood which continued beyond the early months. It can be concluded from these two groups of women that there was a slight decrease in the incidence of depressive symptoms after starting a safe method of contraception. The improvement in mood in the O.C. throughout group may result from relief of premenstrual symptoms (Mears and Grant, 1962; Moos, 1968; Herzberg and Coppen, 1970). An alternative explanation is a "druginduced" feeling of well-being and mild euphoria in some women, similar to the reactions which sometimes follow administration of corticotrophin or cortisone (Eiduson et al., 1964)

The mean depression score of the O.C. stop/change group increased from the first to the second visit, in contrast to the other groups. Fig. 2 shows that 50% of this group had increased scores at the second visit compared with 29% and 24% of the I.U.D. and O.C. throughout groups respectively. The mean depression scores at the third and later visits were lower than the score at the second visit, which indicated that many of the women who experienced adverse changes soon after starting oral contraceptives stopped or changed them with some relief of their symptoms.

The assumption that libido can be measured may be criticized. However, though the rating of three aspects of sexual behaviour—namely, interest, frequency, and satisfaction of intercourse—was by means of a short questionnaire lacking, no doubt, the subtle nature of inquiry by a sympathetic interviewer, the subjects using the different oral contraceptives responded similarly and thus, to some extent, validated the method.

The results in Fig. 3 suggest that starting a safe method of contraception is often followed by increased sexual interest and activity. However, this increase in libido is not maintained in women on oral contraceptives, in contrast to the I.U.D. group, which showed a progressive increase throughout the survey. The women in the O.C. stop/change group showed a slight but progressive decrease in libido throughout the survey. The changes in the O.C. throughout and O.C. stop/change groups support the suggestion that oral contraceptives may have an adverse effect on sexual behaviour (Kane et al., 1967; Nilsson and Solvell, 1967; Nilsson et al., 1967; Michael and Plant, 1969; Huffer et al., 1971).

In some women there was an association between loss of libido and depression; those who stopped oral contraceptives because of loss of libido were significantly more depressed initially than those who gave other reasons for stopping.

However, the progressive improvement in mood in the O.C. throughout group contrasts with the pattern of changes seen in the libido ratings, and indicates that the association between mood and libido in women on oral contraceptives may be complex.

Headaches as a side effect of oral contraceptive medication have been described by several workers (Whitty et al., 1966; British Medical Journal, 1968; Grant and Mears, 1968). In this series the incidence of severe headaches increased in the O.C. total group, in contrast to the I.U.D. group, where, though the incidence was high initially, it did not increase. The increased incidence of severe headaches in the O.C. throughout group is of particular interest, since it contrasts with the progressive improvement in mood found in this group and suggests that headaches are a side effect which women using oral contraceptives tolerate. It is suggested that headaches may be confined to a few days of the menstrual cycle and consequently may be tolerated.

The results from analysing the data obtained at the first clinic visit indicated that the susceptibility of the individual woman to developing symptoms is probably of greater importance than the composition of the oral contraceptive. Significant differences were found between those women who continued and those who stopped or changed oral contraceptives. A history of depression usually severe and prolonged during pregnancy or premenstrually suggests a sensitivity to hormonal changes associated with increased circulating progesterone. The significantly higher neuroticism scores of the O.C. stop/change group supported the findings of Nilsson et al. (1967) and indicated that there was poor adaptive ability in this group. This was also shown in this survey by the more frequent histories of treatment with antidepressants or outpatient psychiatric visits.

## **Conclusions**

In this survey 37% of women remained on the same oral contraceptive for one year. Though they experienced a progressive improvement in mood, they had an increase in incidence of moderate or severe headaches. Twenty-five per cent. stopped using oral contraceptives because of side effects, the most common of which were headaches, depression, and loss of libido. The results suggest that some women in this group can be identified from their histories of depression and severe premenstrual weepiness and, where possible, they should be advised to use alternative methods of contraception.

The I.U.D. was acceptable to 74% of women, the only adverse affect being breakthrough bleeding. The improvement in mood and the increase in libido in the I.U.D. group suggest that this is a safe and acceptable method of contraception.

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## Appendix: Self-rating Scale for Assessing Libido

Below are some groups of statements headed I, II, and III. Begin by reading all the statements in group I, and then mark the one statement that best describes how you have been feeling over the last four weeks. Go through groups II and III in the same way.	Scale II DURING THE LAST FOUR WEEKS  I have had a climax nearly every time I have had intercourse.  I sometimes have a climax but usually enjoy intercourse.  I rarely or never have a climax but enjoy intercourse.  I have little or no sexual feeling.
Scale I	Scale III
DURING THE LAST FOUR WEEKS	DURING THE LAST FOUR WEEKS
I have been much more interested in sex than I used to be.	I have usually had intercourse:
I have been more interested in sex than I used to be.	☐ Three times or more a week.
I have not noticed any change in my interest in sex.	Once or twice a week.
I have been less interested in sex than I used to be.	Less than once a week.
I have been much less interested in sex.	Not had intercourse.