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Experience with Norplant®-2 in Thai women

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ABSTRACT

Two 4.4 cm covered silastic rods, each containing 70 mg levo--norgestrel were studied in 200 women at Siriraj Hospital, Bangkok. Over 90 percent of the women were between 20 to 34 years old, and 88% had 1 to 2 children. The reasons for selecting the implant were preg--nancy spacing (51.5%), complete family size (33 %) and low income (15.5%). Most recent contraceptives prior to the implant were oral pill (55 %), injectable (23 %), condom (5 %) and IUD (2 %). The implant was the first contraceptive used in 12 percent of women. At 24 months of use, the continuation rate was over 90 % which is the highest recorded among all temporary contraceptives. Bleeding patterns were similar to those of the Norplant® silastic capsules. No pregnancy occurred during the period of study. There were no significant changes in body weight, blood pressure, hematocrit, blood glucose, blood urea nitrogen, creatinine, uric acid, and liver function among 10 volunteers studied at six and twelve months of use. However, there was a slight decrease in high density lipoprotein cholesterol which returned to pre--treatment level at one month after implant removal.

Six 3.4 cm. subdermal silastic (polydimethyl siloxane) capsules, each containing 36 mg. of levonorgestrel, have been developed by the Population Council under the trade name of Norplant®. Norplant® subdermal implants have been widely studied and was proved to be safe and highly effective for up to five years.[1,2,3,4] Because of its apparent program--matic advantage, the Thai National Family Planning Program initiated a pilot Norplant® study in different parts of the country in 1980. Though the initial physicians' response was rather negative because of the size and number of the implant capsules needed, this method was proved to be well accepted by Thai women and had the highest continuation rate among all available reversible contraceptives.[5] However, removal of six capsules could become a burden in a busy family planning clinic if this method were being used in a large national program.

The Norplant®-2 covered rod system comprises 2 silastic rods and has been shown to produce slightly higher blood level of levonorgestrel than those produced by Norplant six capsules. A constant level of levo--norgestrel was expected to be maintained for over five years[6]. This new two-rod implant should therefore be expected to be as effective as the six-capsule Norplant®.

This trial was planned to study the efficacy, undesirable effects and the acceptability of this new, covered rod implant.

MATERIALS AND METHODS

The Norplant®-2 covered rod system

The covered rod system used in this study consisted of two silastic rods of 4.4 mm length and 2.4 mm outside diameter which are a homogenous mixture of silastic and crystaline levonorgestrel 70 mg. per rod, encased in thin-walled silastic tubing.

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Insertion site

The two covered rods were placed in a fan like manner in the inner upper left arm with the 'fan' opening away from the elbow. The insertion point was about 10 cm from the elbow. The patient lay down on the bed, left arm extended at a right angle to the body.

Insertion technique

Under the sterile technique, local infiltration of xylocaine 1 % was done by inserting the needle at the implant insertion point. The xylocaine was injected subdermally into two lines corresponding to the place where the implants would be inserted. The total xylocaine used was 4 ml. A one millimeter incision was made at the point of insertion. A number 10 trocar was inserted through the skin incision until the open end of the trocar was beneath the skin. The trocar was then pointed toward the skin and was advanced just beneath and parallel to the skin until the upper mark on the trocar reached the skin incision. The first implant was loaded into the trocar and was gently pushed along the channel by the plunger until the implant stopped. The plunger was held firmly in place and the trocar drawn back until the lower mark of the trocar became visible, indicating that the implant was unloaded. The same procedure was repeated for the second implant in a fan-like form. The trocar was then withdrawn. The incision was pressed down with a gauzed finger to stop oozing and a small bandage was placed over the skin incision. To minimize the post-insertion ecchymosis, an elastic bandage was applied over the incision for a few hours.

Removal technique

Under sterile conditions, 2-3 ml of xylocaine 2% was injected just beneath the implant. A 2 mm incision was made close or slightly above the previous incision, close to the lower end of both implants. One implant was moved, using thumb pressure just under the lower end of the implant (near the skin incision), with the index finger pushing the upper end toward the incision until the lower end was felt through the incision. The lower end of the implant was then grasped with small non-toothed hemostat forceps. The fibrous tissue covering the exposed implant end was dissected with a scalpel until the implant was free and had popped through the in--cision. The implant was then easily pulled out. The same procedure was repeated to remove the second rod. A single stitch was occasionally necessary to close the skin properly.

Subject selection

Two hundred patients were recruited between October 27, 1983 to October 21, 1985 for clinical study.

The following criteria were used for selection of the subjects:

1) Age between 18 - 40
2) No contraindication to the use of steroidal contraceptives
3) Have had at least one live birth
4 Regularly exposed to the risk of pregnancy
5) Not currently pregnant
6) Not currently breast-feeding
7) Willing to participate in the study and be accessible for follow-up

An addtional 10 volunteers were also recruited for metabolic and

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Admission procedure:

Patients were informed about the Norplant®-2 system, stressing its advantages and disadvantages, before accepting this method. All patients got routine general physical examinations including Papanicolaou Smear and routine laboratory check.

Follow-up

The patients were advised to come for follow-up visits at 4 - 7 days, 3 months, and 6 months after insertion, and every 6 months there--after. They were also advised to record their bleeding in a menstrual diary card. The implant would be removed 5 years after insertion or earlier if the patient requested.

RESULTS

(Table 1,2,3)

Acceptors' characteristics

As shown in Tables 1 and 2, the majority of the acceptors were between 20 to 29 years old (72%) and had one to two living children (88%). As the clinic generally serves the lower socio-economic population, the majority of the acceptors (65%) had primary education, 32% had completed secondary or vocational school level and only three percent passed university level (Table 3).

(Table 4)

Their most recent contraceptive used were oral pill (55%), injectable (26%), condom (5%) and IUD (2%) (Table 4). Twenty-four women (12%) had not used any contraceptive before accepting Norplant®-2.

(Table 5)

As shown in Table 5, the main reasons for requesting contraception

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Source of information

(Table 6)

Table 6 shows the source of information on Norplant®-2. Because of limited supplies of the covered rods, the hospital did not publicize this method except by having one information poster displayed in the clinic waiting room. Friends and relatives who had heard about this method were the major source of information (41%). Hospital staff were the second major source (19%). Previous implant users (15%) and other family planning acceptors (15%) were also important sources of information.

Localized Reaction

(Table 7)

Localized reaction to the rods within the first seven days and 3 months are shown in Table 7. All patients did not have to stop their routine daily work. During the first seven days after placement of the implant, 14 women (7%) felt slight discomfort and 2 women (1%) had mild pain over the insertion site. Ecchymosis was observed in 15 women (7.5%). Seven women (3.5%) experienced itching around the incision. One case was allergic to the adhesive plaster. No local infection or inflammation was observed. Of 199 patients followed at 3 months after insertion, nine women (4.5%) complained of mild discomfort and three women (1.5%) had mild pain. When the lesion was palpated, there was no sign of inflam--mation. Palpation of the implants was painless in all women. Five women (2.5%) complained of occasional itching at the insertion site.

Menstrual patterns

Bleeding patterns were studied using the Rodriguez method[7] at 90 day intervals (reference period), although not all women completed their

menstrual diary records as advised. The number of menstrual records available for study in the first, second, third and fourth reference periods are 111, 104, 104 and 103 respectively.

Amenorrhoea

(Table 8)

Table 8 shows the percentage of users with amenorrhoea of 46-89 days interval and total amenorrhoea throughout the 90 -day reference period. The percentage of total amenorrhoea in the users in each reference period varied from 27% to 37%. There was no tendency toward increased amenorrhoea in the first three years of use.

Bleeding episodes

(Table 9)

Details of bleeding are shown in Table 9. For simplicity, both bleeding and spotting were defined as bleeding. The mean number of bleeding episodes per 3-month interval (excluding intervals with total amenorrhoea) was rather constant across all reference periods (2.3 - 2.7 per interval).

The mean episode length was approximately 6 days in all reference periods, though the standard deviations are substantial.

The mean cycle length in the four reference periods of study did not differ significantly from each other (24-30 days), although the standard deviation was high in all study periods (12-17 days).

The mean total number of days of bleeding and spotting occurring within three months of the reference period was between 13-16 days with the standard deviation of 12 to 16 days.

Bleeding observed by most patients was usually light. Heavy bleeding was reported by only two women, one in the third reference period (month 7-9) and another in the fourth reference period (month 10-12).

On interviewing 199 cases at 6-9 months after insertion, 83 women (42%) considered that their menstrual patterns were normal.

Failures:

Up to the time of this report (July 31, 1986) there were 4,173 woman months of use. So far, no pregnancy has been observed.

Continuation rates:

(Table 10)

Net cumulative continuation rates through the first two years after insertion are shown in table 10. The continuation rates per 100 acceptors after 12 and 24 months of use were 94.7 and 92.8 respectively.

(Table 11)

During the study period (October 1983 - July 1986), there were 17 removals, (Table 11). Among these, four are for medical reasons: prolonged spotting (1), prolonged amenorrhoea (1), weight gain (1) and nervousness, fatigue (1). One woman complaining of nervousness and fatigue informed that she was also afraid of the method because this method was criticized by a physician on a television health program.

Of eight women who requested removal for planning pregnancy, three women had used the method for over two years, three women had used the method between one to two years, and two women had used the method for less than one year. The reasons for early desire for pregnancy in the latter two women were that one woman had remarried and the other woman's husband wanted another child before he went abroad.

One out of two women who changed to tubal sterilization also complained of occasional pain at insertion site, which might partly be the reason for changing of method. One woman requested removal after her husband had vasectomy. Other two personal reasons for removal were husband died (1) and divorced (1).

Removal of the Norplant®-2 was much easier than that of the Norplant® and required less than ten minutes.

Metabolic studies

Study in ten volunteers showed no significant changes in body weight, blood pressure, hematocrit, blood glucose, blood urea nitrogen, creatinine, uric acid, and liver function at six and twelve months of use. However, there was a slight decrease in high density lipoprotein cholesterol which returned to pretreatment level at one month after implant removal. Details of hormonal and metabolic studies will be presented in a separate paper.

CONCLUSION

The first-three year results among the Norplant®-2 users are very promising. The local effects have been minimal. The main side effects are bleeding irregularities and amenorrhoea, though 42% of the patients considered their bleeding patterns as normal. The efficacy of Norplant®-2 during the first two to three years of use was satisfactory. Further follow-up is needed to confirm five-year efficacy. It is obvious that Norplant®-2 has advantage over Norplant® as it is much easier to both insert and remove the two covered rods. Norplant®-2 should then be well-adapted to a nationwide program should further follow-up to 5 year result be satisfactory.

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Table 1. Age groups of Norplant®-2 acceptors

Age group	No.	%
24	87	43.5
25 - 29	64	32.0
30 - 34	37	18.5
35 - 39	12	6.0
Total	200	100

Table 2. Parity of Norplant®-2 acceptors

Parity	No.	%
1	102	51.0
2	75	37.5
3	18	9.0
4	5	2.5
Total	200	100

Table 3. Educational levels

Education	No.	%
Primary	130	65.0
Secondary	34	17.0
Vocational	30	15.0
University	6	3.0
Total	200	100

Table 4. Most recent contraceptive used

methods	No.	%
Pill	110	55.0
Injectable	52	26.0
Condom	10	5.0
IUD	4	2.0
None	24	12.0
Total	200	100

Table 5. Reasons for contracepting

Reasons	No.	%
Spacing	103	51.5
Enough children	66	33.0
Financial	31	15.5
Total	200	100

Table 6. Source of information on implant

Sources	No.	%
Friends and relatives	82	41.0
Hospital staff	39	19.5
Family planning acceptors	31	15.5
Norplant users	30	15.0
Mass media	18	9.0
Total	200	100

Table 7. Local reaction

Signs and symptoms	Time after insertion			
	7 days		3 months	
	No.	%	No.	%
Discomfort	14	7.0	9	4.5
Pain	2	1.0	3	1.5
Itching	7	3.5	5	2.5
Ecchymosis	15	7.5	-	-
Allergic to adhesive plaster	1	0.5	-	-
None	161	80.5	182	91.5
Total	200	100.0	199	100.0

Table 8. Incidence of amenorrhea by reference periods

Reference periods	No. of women	women with total amenorrhea		women with 46-89 days amenorrhea		women with no amenorrhea	
		No.	%	No.	%	No.	%
1 (month 1-3)	111	30	27.0	48	43.2	33	29.7
2 (month 4-6)	104	39	37.5	37	35.6	28	26.9
3 (month 7-9)	104	39	37.5	36	34.6	29	37.9
4 (month 10-12)	103	31	30.1	32	31.1	40	38.8

Table 11 Reasons for 17 removals

Reasons	No.
Medical	
Prolonged spotting	1
Prolonged amenorrhoea	1
Weight gain	1
Fatigue, nervousness*	1
Personal	
Planning pregnancy	8
Change to female sterilization	2
Husband had vasectomy	1
Husband died	1
Divorced	1
Total	17

* probably resulting from adverse publicity.

BRIEF REPORT ON THE STUDY OF SERUM LEVEL OF LEVONORGESTREL IN NORPLANT®-2 USERS.

POPULATION COUNCIL AWARD NO. 184.06A:

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Ten female volunteers were recruited from hospital workers using the following criteria:

1. age: 20-39 years,
2. having normal menstrual period within the past 6 months,
3. no steroidal treatment within the past 6 months,
4. no contraindication to the use of Norplant,
5. willing to participate in the study.

Norplant®-2 insertion:

- Norplant®-2 were inserted at the inner side of the upper arm within the first 5 days of the menstrual cycle and were retained up to 12 months after insertion.

Physical examination and laboratory tests:

- Physical examination was performed before Norplant®-2 insertion, and at 6 and 12 months thereafter.
- Pelvic examination including PAP Smear was performed before Norplant®-2 insertion and at 12 months after insertion.

Laboratory tests:

Hematocrit, BUN, creatinine, uric acid, SGOT and SGPT were carried out before Norplant®-2 insertion and at 6 and 12 months thereafter.

Serum cholesterol, triglycerides, HDL-C and LDL-C were detected before Norplant®-2 insertion and at 3,4,5,6,7,8,9,10,11, 12 months thereafter and at 1 month after removal.

Hormonal study:

Serum levonorgestrel and progesterone were detected at the 20th day of the controlled cycles and at 1,2,3,4,7,14,28,42,56,70,84,98,112, 126,140,154,168,196,224,252,280,308,336 days after insertion and at 7,14,21 and 28 days after removal.

Bleeding patterns and other clinical signs and symptoms were also recorded.

Results:

It is planned that report of the results of level of levonorgestrel among 10 volunteers during the first 12 months of use will be presented together with the serum level of levonorgestrel at the end of second, third and fourth years of the clinic patients.

The results among 10 volunteers are first shown in table 1 - - -

Table 1. Age groups of the volunteers

Age group	No. of cases
20 - 24	3
25 - 29	2
30 - 34	2
35 - 39	3
Total	10

Table 2. Body Weight (kg.) before and after Norplant®-2 insertion

Case No.	Control	6th month	12th month
1	52	53.5	53.2
2	51	53.8	56
3	44.1	44	43.3
4	53.5	52	53.6
5	50	49.5	50
6	47	48.4	48.6
7	62.5	64	65
8	45.3	45	48
9	50.5	51.8	53.8
10	44	43.5	43.5
Mean	49.9	50.5	51.5
S.D.	5.5	6.1	6.4

Table 3. Blood pressure before and after Norplant®-2 insertion

Case No.	Control		6th month		12th month	
	Systolic	Diastolic	Systolic	Diastolic	Systolic	Diastolic
1	90	52	90	60	92	50
2	104	66	100	70	94	50
3	104	62	90	62	100	70
4	100	60	90	60	90	50
5	120	70	110	74	102	72
6	90	52	90	50	80	50
7	120	70	120	90	126	76
8	104	50	100	70	94	58
9	100	56	90	52	108	58
10	110	66	100	70	90	60
Mean	104.2	60.4	98.0	65.8	97.6	59.4
S.D.	10.4	7.6	10.3	11.7	12.6	10.0

Table 4. Hematocrit value before and after Norplant®-2 insertion.

Case No.	Control	6th month	12th month
1	37	40	39
2	35	38	39
3	36	32.5	37
4	36	37	38
5	37	40	41
6	37	39	40
7	40	35	36
8	40	44	42
9	40	39	35
10	42	42	39
Mean	38	38.6	38.6
S.D.	2.3	3.3	2.2

Table 5. Fasting blood glucose (mg %) before and after Norplant®-2 insertion.

Case No.	Control	6th month	12th month
1	90	90	100
2	100	95	100
3	100	80	105
4	85	95	95
5	110	100	90
6	90	95	95
7	105	95	95
8	105	100	95
9	90	95	110
10	100	80	90
Mean	97.5	92.5	97.5
S.D.	8.2	7.2	6.3

Table 6. BUN (mg %) before and after Norplant®-2 insertion.

Case No.	Control	6th month	12th month
1	12	15	15
2	12	13	10
3	12	10	13
4	8	13	9
5	13	11	14
6	12	16	13
7	10	12	11
8	14	11	8
9	11	13	8
10	14	12	18
Mean	11.8	12.6	11.9
S.D.	1.8	1.8	3.3

Table 7. Creatinine (mg %) before and after Norplant®-2 insertion

Case No.	Control	6th month	12th month
1	1.0	0.9	1.0
2	1.0	0.8	0.8
3	1.1	0.9	0.7
4	0.7	0.9	0.8
5	0.7	0.7	0.8
6	0.8	0.8	0.9
7	1.0	0.9	0.7
8	1.0	1.1	0.6
9	0.8	1.1	0.8
10	0.7	0.8	1.0
Mean	0.9	0.9	0.8
S.D.	0.1	0.1	0.1

Table 8. Uric acid (mg %) before and after Norplant®-2 insertion.

Case No.	Control	6th month	12th month
1	4.5	5.1	5.3
2	4.8	4.7	4.8
3	6.2	6.3	6.5
4	4.7	4.3	5.0
5	6.1	5.0	5.7
6	4.6	5.0	4.7
7	7.0	6.0	5.0
8	5.5	5.5	4.3
9	4.8	5.4	5.0
10	2.4	3.0	2.2
Mean	5.1	5.0	4.8
S.D.	1.2	0.9	1.1

Table 9. SGOT (Sigma Fronkel unit) before and after Norplant®-2 insertion.

Case No.	Control	6th month	12th month
1	21	14	16
2	17	17	14
3	17	17	17
4	18	21	16
5	21	23	18
6	13	17	18
7	10	17	10
8	23	19	26
9	21	21	16
10	28	19	14
Mean	18.9	18.5	16.5
S.D.	5.1	2.6	4.1

Table 10. SGPT (Sigma Raankel Unit) before and after Norplant®-2 insertion.

Case No.	Control	6th month	12th month
1	10	10	7
2	25	11	15
3	8	9	10
4	14	13	8
5	32	12	12
6	10	10	9
7	10	8	8
8	22	8	8
9	13	7	8
10	13	12	11
Mean	15.7	10.0	9.6
S.D.	7.9	2.0	2.4

Table 11. Cholesterol level (mg %) before and after Norplant®-2 insertion.

Months after insertion \ Case No.	1	2	3	4	5	6	7	8	9	10	Mean	S.D.
Control	187	189	187	155	182	164	201	199	200	179	184.3	15.2
3	161	168	-	158	133	165	154	162	150	140	154.5	11.7
4	150	152	168	147	162	146	183	156	186	98	154.8	24.5
5	151	180	162	147	165	171	170	170	165	153	163.4	10.3
6	167	205	149	195	191	172	212	200	193	155	183.9	21.7
7	158	165	141	169	191	147	237	177	190	169	174.4	27.3
8	150	180	155	135	143	145	177	167	153	160	156.5	14.6
9	137	177	160	144	143	157	156	156	165	160	155.5	11.7
10	145	163	179	154	153	129	168	154	128	138	151.1	16.5
11	172	193	142	160	180	203	180	190	165	166	175.1	17.9
12	137	223	170	170	144	135	215	185	144	190	171.3	31.8
13	159	195	150	152	135	100	172	178	175	165	158.1	26.4

Table 12. Triglyceride level (mg %) before and after Norplant®-2 insertion

Case No / Trigly-ceride	1	2	3	4	5	6	7	8	9	10	Mean	S.D.
Control	95	105	74	90	83	129	114	75	73	114	95.2	19.6
3	65	78	-	66	64	94	95	53	61	75	72.3	14.5
4	81	103	85	84	88	74	85	81	77	90	84.8	8.0
5	56	70	90	75	74	75	58	71	64	63	69.6	9.9
6	83	61	66	91	71	78	75	88	80	85	77.8	9.6
7	93	73	71	81	101	80	88	74	74	70	80.5	10.4
8	57	75	80	115	108	81	122	92	101	87	91.8	19.9
9	66	75	64	92	103	91	90	85	85	90	84.1	12.3
10	77	75	83	85	83	97	77	81	70	73	80.1	7.6
11	91	90	84	61	51	88	80	88	65	73	77.1	14.0
12	71	95	85	71	73	85	84	71	64	57	75.6	11.4
13	84	94	64	75	139	80	77	70	78	80	84.1	20.9

Table 13. HDL-C (mg %) before and after Norplant®-2 insertion.

HDL-C \ Case No.	1	2	3	4	5	6	7	8	9	10	Mean	S.D
Control	61.9	43.9	61.9	39.4	50.6	56.3	39.4	61.9	61.9	81.0	55.8	12.
3	45.8	39.7	34.6	37.0	42.5	43.6	30.3	51.3	54.6	36.0	41.5	7.
4	29.2	41.6	37.7	28.9	32.0	40.6	34.2	41.0	41.0	33.1	35.9	5.
5	44.9	37.7	32.0	30.7	37.7	35.7	34.2	46.7	42.3	39.5	38.1	5.
6	45.2	47.8	43.2	39.9	40.8	39.5	30.5	49.5	50.2	37.9	42.4	6.
7	46.7	41.2	37.0	36.6	28.9	39.9	38.4	46.9	46.0	41.6	40.3	5.
8	41.4	46.9	40.8	30.0	34.6	38.6	34.6	43.8	46.0	37.3	39.3	5.
9	39.5	48.2	23.0	33.6	33.2	40.3	29.4	42.2	46.4	39.5	37.5	7.
10	44.5	47.4	37.3	32.9	35.1	36.2	34.2	47.6	40.8	38.4	39.4	5.
11	48.4	46.9	37.9	39.0	39.0	44.5	37.3	52.2	43.0	42.1	43.0	5.
12	45.8	46.5	41.6	35.1	36.4	41.0	34.0	33.8	48.0	48.9	41.1	6.
13	46.0	57.9	54.8	31.4	43.4	53.9	31.8	61.2	59.8	61.4	50.2	11.

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Table 14. LDL-C (mg %) before and after Norplant®-2 insertion

LDL-C \ Case No.	1	2	3	4	5	6	7	8	9	10	Mean	S.
Control	106.1	124.1	110.3	97.6	114.8	81.9	138.8	122.1	123.4	75.2	109.4	19
3	102.2	112.7	-	107.8	77.7	102.6	104.8	100.1	83.2	89.9	97.9	11
4	104.7	89.8	113.3	101.3	112.4	90.6	131.8	98.8	129.6	46.9	101.9	24
5	94.9	128.3	112.0	101.3	112.5	120.3	124.2	109.1	109.9	101.0	111.3	10
6	105.3	145.0	92.6	136.9	136.0	117.0	166.5	132.9	126.8	100.1	125.9	22
7	92.7	109.2	89.8	116.2	141.9	91.1	181.0	115.3	129.2	113.4	118.0	27
8	97.2	118.1	98.2	82.0	86.8	90.2	118.0	104.8	86.8	105.3	98.7	12
9	84.4	113.8	124.2	92.0	89.2	98.5	108.6	96.9	101.6	102.6	101.2	11
10	85.1	100.7	125.1	104.1	101.3	73.4	108.4	90.2	73.2	85.0	94.6	16
11	105.4	128.1	87.3	108.8	130.8	140.9	126.7	120.2	109.0	109.3	116.6	15
12	77.0	157.5	111.4	120.7	93.0	77.0	164.2	137.0	83.2	129.7	115.1	32
13	96.2	118.3	82.4	105.6	63.8	30.1	124.8	102.8	99.6	87.6	91.1	27

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Table 15. Levonorgestrel level (n mol/L) during the 12 months period of Norplant®-2 use and after removal.

Days after insertion \ Case No.	1	2	3	4	5	6	7	8	9	10	Mean
1	1.7	3.2	2.7	2.1	0.88	2.6	0.9	3.3	1.9	1.9	2.1
2	1.9	3.5	3.3	2.9	0.85	3.4	1.1	4.5	2.0	2.2	2.6
3	1.9	3.5	3.1	2.4	0.9	3.6	1.1	4.3	1.7	2.3	2.5
4	2.0	3.7	2.8	2.7	1.1	3.6	0.98	3.4	2.1	2.2	2.4
7	2.1	-	2.5	2.8	1.3	3.1	0.88	3.4	2.0	1.7	2.2
14	1.7	2.6	1.9	2.9	1.3	2.0	1.8	2.2	2.0	1.7	2.0
28	1.5	2.1	1.4	1.9	1.1	2.1	1.0	1.7	1.5	1.1	1.5
42	1.4	1.8	1.6	2.0	1.1	1.6	1.2	2.2	1.6	1.1	1.6
56	1.5	2.2	1.4	2.1	0.95	1.8	1.3	2.2	1.7	1.2	1.6
70	1.2	1.9	1.3	1.5	0.82	1.8	1.1	2.0	1.5	1.2	1.4
84	1.2	1.8	1.3	1.6	0.9	1.9	1.4	2.0	1.7	0.9	1.5
98	1.6	1.7	1.5	1.8	0.97	1.7	1.1	1.8	1.5	1.0	1.5
112	1.3	1.8	1.4	1.5	0.93	1.6	1.0	2.0	1.4	0.95	1.4
126	1.2	2.1	1.4	1.6	0.95	1.5	1.2	1.6	1.4	0.95	1.4
140	1.3	1.4	1.4	1.8	0.78	1.6	0.87	1.5	1.5	1.1	1.3
154	1.4	1.5	1.4	2.0	0.71	1.6	1.2	1.8	1.3	1.2	1.4
168	1.1	1.4	1.8	1.7	0.92	1.4	0.97	2.1	1.2	0.95	1.3
196	1.1	1.6	1.3	1.5	0.97	1.5	0.96	1.8	1.2	0.98	1.3
224	1.2	1.5	1.1	1.3	0.8	1.6	1.2	2.1	1.2	1.1	1.3
252	1.1	1.4	1.5	1.4	0.79	1.5	1.1	1.9	1.3	1.0	1.3
280	1.1	1.1	1.3	2.2	0.83	1.5	0.94	1.6	1.6	0.93	1.3
308	1.1	1.2	1.2	1.4	0.76	1.6	0.91	1.6	1.6	0.83	1.2
336	1.0	1.1	1.3	1.6	0.72	1.3	0.97	2.2	1.5	0.52	1.2
Days after removal											
7	0.16	0.19	0.16	0.16	0.16	0.17	0.24	0.16	0.16	0.16	
14	0.16	0.16	-	0.16	0.16	0.16	0.16	0.16	0.16	0.16	
21	0.16	0.16	0.16	0.16	0.16	0.16	0.16	0.16	0.16	0.16	
28	0.16	-	0.16	0.16	0.16	0.16	0.16	0.16	0.16	0.16	

Table 16. Progesterone (n mol/L) during the 12 months period of Norplant®-2 use and after removal.

Days after insertion \ Case No	1	2	3	4	5	6	7	8	9	10
Control	27.0	9.0	40.0	< 1.6	< 1.6	29.0	36.0	56.0	42.0	< 1.6
1	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6
2	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6
3	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6
4	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6
5	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6
6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6
7	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6
8	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6
9	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6
10	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6
11	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6
12	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6
13	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6
14	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6
15	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6
16	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6
17	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6
18	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6
19	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6
20	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6
21	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6
22	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6
23	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6
Days after removal										
7	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6
14	< 1.6	< 1.6	< 1.6	46.0	12.1	< 1.6	< 1.6	< 1.6	< 1.6	< 1.6
21	33.0	< 1.6	30.5	< 9.5	< 1.6	11.2	< 1.6	26.5	< 1.6	< 1.6
28	< 1.6	15.2	< 1.6	< 1.6	< 1.6	14.0	< 1.6	< 1.6	< 1.6	< 1.6