

PN-ABF-625  
67200

# AGENCY FOR INTERNATIONAL DEVELOPMENT PPC/CDIE/DI REPORT PROCESSING FORM

ENTER INFORMATION ONLY IF NOT INCLUDED ON COVER OR TITLE PAGE OF DOCUMENT

1. Project/Subproject Number 9363041	2. Contract/Grant Number DPE-CA-4047-00	3. Publication Date June 1989
---	--	----------------------------------

4. Document Title/Translated Title

Norplant contraceptive subdermal implants:  
two year experience in Singapore

5. Author(s)

1. Singh, K.
2. Viegas O.A.C.
3. Singh, P.
4. Ratnam, S.S.

6. Contributing Organization(s)

Family Health International

7. Pagination 9 p.	8. Report Number 89-33	9. Sponsoring A.I.D. Office
-----------------------	---------------------------	-----------------------------

10. Abstract (optional - 250 word limit)

11. Subject Keywords (optional)

1. NORPLANT	4. <i>continuation</i>
2. <i>menstruation</i>	5.
3. <i>side effects</i>	6.

12. Supplementary Notes

13. Submitting Official <i>Debbie Wade</i>	14. Telephone Number 919-544-7040	15. Today's Date 3-20-90
---	--------------------------------------	-----------------------------

.....DO NOT write below this line.....

16. DOCID	17. Document Disposition DOCRD [] INV [] DUPLICATE []
-----------	--

## Norplant<sup>®</sup> contraceptive subdermal implants: two-year experience in Singapore

K. SINGH, O.A.C. VIEGAS, P. SINGH and S.S. RATNAM

*Department of Obstetrics and Gynaecology, National University of Singapore, National University Hospital, Lower Kent Ridge Road, Singapore 0511*

### Abstract

Norplant contraceptive implants are Silastic containing levonorgestrel implants. This study describes our two-year experience with 100 acceptors of Norplant implants in Singapore. No pregnancies occurred during the first two years of use. Desire for planned pregnancy and disruption of menstrual rhythm were the two main reasons for twenty implant removals during the two years. The continuation rate at the end of two years was 79%. The post-removal conception rate in women desiring pregnancy was 90% at the end of one year. It thus appears that the Norplant contraceptive system offers a highly effective, acceptable, reversible and safe method of contraception.

### Introduction

The Norplant system (subdermal implants) consists of six Silastic capsules, each containing 36 mg of levonorgestrel and having a diameter of 2.4 mm and a length of 3.4 cm. It is one of the most modern hormonal fertility regulating methods that is effective for five years and it is currently undergoing clinical trials at the fertility control clinic, National University Hospital, Singapore. This ongoing study attempts to evaluate the efficacy, acceptability and safety of this method of contraception. This paper presents our results at the end of two years of Norplant use.

### Methodology

Enrollment of subjects began in May 1985 and 100 women were recruited by November 1985. This report is based on data from clinic visits through October 1988.

In recruiting acceptors, we used criteria set by the Population Council's International Committee for Contraception Research. Acceptors were between 18 and 40 years of age, sexually active, of demonstrable fertility (at least one birth), neither pregnant nor breastfeeding at the time of insertion, and had no standard contraindications to the use of steroids. They had to be easily followed-up on a

regular basis and also were requested to use no other contraceptive during the study. All women gave full informed consent and met the criteria established by the National University Hospital's ethical committee.

Follow-up of all acceptors was scheduled at 1, 3, 6, 12, 18 and 24 months after admission to the study, although the women were encouraged to return to the clinic for any problems that occurred at any time, regardless of the next scheduled follow-up visit. Follow-up of all acceptors at each scheduled visit in the first two years was 100%.

## Results

### *Pregnancy*

No pregnancy occurred during the first two years of use.

### *Termination and continuation*

A total of 21 removals were reported in the first two years of use. Ten devices were removed from women due to planned pregnancy and another 10 were removed for menstrual disturbances. There was only one removal for non-menstrual problems.

Of the ten removals due to menstrual disturbances, seven were in women who complained of prolonged bleeding or spotting lasting more than 10 days. Of these seven, 57.1% (four women) had bleeding or spotting lasting more than 31 days. Another two women had the implants removed due to increased frequency of menstruation. Only one woman had the implants removed for prolonged amenorrhea. The only removal for non-menstrual problems was from a woman who had a weight loss of 7 kg over a period of 18 months.

On subsequent follow-up, the menstrual pattern had returned to normal in all the ten women who had removals for menstrual disturbances. At one year post-removal, however, the weight had still not increased in the woman who had the implants removed for weight loss.

The two-year cumulative life table rates are presented in Table 1. The net termination rate was 21 per 100 women at two years. The continuation rate was 79%.

### *Changes in weight, blood pressure and menstrual changes*

Changes in body weight, blood pressure, menstrual cycle length and menstrual flow duration at the end of two years in the same set of women are shown in Table 2. There was an average 1.7 kg increase in weight after two years of use. There was a 2.4 mmHg increase in systolic blood pressure and a 0.9 mmHg increase in diastolic blood pressure. Mean cycle length increased slightly over the same period while menstrual flow decreased by 0.7 days. Since irregular menstrual cycles and amenorrhea may occur with the use of Norplant implants, only women whose cycles

were reported to be regular are included in this evaluation of cycle length and flow duration changes.

None of the changes in body weight, blood pressure, menstrual cycle length and menstrual flow duration was statistically significant.

**Table 1** Two-year cumulative life-table rates (per 100 women) for Norplant acceptors in Singapore

<i>Event</i>	<i>Rate*</i>
Pregnancy	0.0
Removals for:	
Desired pregnancy	47.6 (10)
Menstrual problems	47.6 (10)
Weight loss	4.8 (1)
Continuation	79.0
Woman-months	2209.0

\* Numbers of events reported are in parentheses

**Table 2** Changes in clinical measures at two-year follow-up visit for Norplant acceptors in Singapore

<i>Clinical measure</i>	<i>Net change in measure*</i>
Weight (kg)	+1.7 (78)
Systolic blood pressure (mmHg)	+2.4 (78)
Diastolic blood pressure (mmHg)	+0.9 (78)
Menstrual cycle length (days)	+0.3 (69)
Menstrual flow duration (days)	-0.7 (69)

\* Values indicate the mean change from admission to the two-year follow-up visit. Numbers in parentheses indicate number of cases evaluated

### *Adverse experiences*

An adverse experience is defined as any complication or complaint by the acceptor. A listing of all adverse experiences reported by the women during any follow-up visit appears in Table 3. Only 16.5% of acceptors reported one or more adverse events

---

during their second year of Norplant use as compared to 57.0% during the first year of use [1]. In the second year there were only two scheduled clinical visits as compared to four visits in the first year, however patients were encouraged at all times to come for unscheduled visits, should they have any complaints. As such, it would appear that the putative decline in the frequency of adverse experiences from year 1 to year 2 is not related to the less frequent clinical visits in the second year. Moreover, since each acceptor could have reported more than one adverse experience at any one visit or at different visits, the total number of events in this table exceeds the total number of women with adverse experiences.

The most frequently reported non-menstrual adverse experience in the second year was an increase in body weight (six cases) and yet there were no removals due to this adverse experience. There was in fact one removal due to a weight loss of 7 kg over 18 months of use. The other adverse experiences reported are shown in Table 3 and are less frequent than those reported in the first year.

An ovarian cyst diagnosed at one woman's first year follow-up visit remained the same size during the second year of use. She had remained amenorrheic for the first 13 months after insertion of the implants. Subsequently her menses returned and have been regular ever since. She refused to have the implants removed or undergo laparotomy for the ovarian cyst. The cyst has remained the same size on ultrasound examination.

#### *Menstrual pattern changes*

Each woman participating in the study was asked to keep a daily record of her menstrual bleeding events, coding '0' for no bleeding, '1' for spotting or light bleeding (but no sanitary protection needed) and '2' for heavy bleeding (sanitary protection needed). Data of the daily bleeding calendar are based upon completed 90-day intervals or reference period. For purposes of analysis, a bleeding run is defined as an unbroken group of bleeding or spotting days beginning with a bleeding day. Bleeding calendar data are summarized in Tables 4 and 5.

The percentage of women reporting prolonged bleeding (8+ days in a run) continued to decrease in the second year of use, to reach 25.3% in the eighth reference period. Similarly, the percentage of women with numerous bleeding days (21+ days) and numerous bleeding and/or spotting days (31+ days) decreased to reach 5.1% and 3.6% in the eighth reference period. In the first two years, seven women had their implants removed due to prolonged bleeding or spotting of more than 10 days.

The percentage of women reporting infrequent bleeding (<2 runs) continued to decline in the second year and was 8.5% in the eighth period. Similarly, the percentage of women with amenorrhea (60+ days) decreased in the second year and was below 10.0% in the last four periods under review. Likewise, the percentage of women reporting few bleeding days (<5 days) decreased and was below 6.0% in the last four periods under review. Only one woman had the implants removed for prolonged amenorrhea of 40 days after having had scanty menses in the first three reference periods following insertion.

Table 3 Adverse experiences reported at follow-up visits by Norplant acceptors

<i>Adverse experience/number reported</i>	<i>Year 1</i>	<i>Year 2</i>
<i>Body as a whole</i>		
Abdominal pain	7	
Chest pain	6	
Chills	3	
Sleepiness	5	
Weakness/fatigue	8	1
<i>Breast</i>		
Breast pain	1	
<i>Digestive system</i>		
Anorexia	6	
Increase in appetite	3	
Nausea	4	
<i>Insertion site</i>		
Hematoma	1	
Local reaction	19	
Implants visible		2
<i>Metabolic and nutritional</i>		
Weight increase	6	6
Weight loss	10	2
<i>Musculoskeletal system</i>		
Arm pain	6	1
Back pain	4	
Numbness/weakness in arm/hand	5	
Weakness in legs	1	
<i>Nervous system</i>		
Dizziness/giddiness	14	2
Headache/head pain	4	3
Insomnia/sleeplessness	4	
Nervousness	1	
<i>Respiratory system</i>		
Breathlessness	5	
<i>Skin and extremities</i>		
Acne	1	
Alopecia	3	
Pruritus	1	1
Skin rashes	3	1
Ulcers in mouth	1	
<i>Urogenital system</i>		
Cervical lesion	1	
Enlarged uterus	1	
Ovarian cyst	3	
Vaginal discharge/itch	7	3
Total number of adverse experiences reported	134	22
Total number of women reporting adverse experiences	37	16

\* This tabulation represents all adverse experiences reported at any follow-up visit. It should be noted that any individual woman could report multiple adverse experiences at any given follow-up visit or at different visits, and each occurrence would appear in this table.

**Table 4** Increased frequency of menstruation and prolonged bleeding/spotting among Norplant acceptors in Singapore by reference period

Reference period	Frequency bleeding 5+ runs (%)	Prolonged bleeding 8+ days (%)	Numerous bleeding 21+ days (%)	Numerous bleeding and/or spotting days 31+ days (%)
1	3.0	48.0	18.0	46.0
2	3.1	41.8	11.2	31.6
3	5.3	30.9	6.4	24.5
4	5.4	30.5	6.8	20.3
5	4.2	28.4	7.4	6.3
6	2.3	27.2	6.8	5.7
7	1.2	26.5	6.0	3.6
8	1.2	25.3	5.1	3.6

**Table 5** Decreased frequency of menstruation and amenorrhea among Norplant acceptors in Singapore by reference period

Reference period	Infrequent bleeding < 2 runs (%)	Amenorrhea of 60+ days (%)	Few bleeding days < 5 days (%)
1	42.0	13.0	39.0
2	44.9	20.4	42.0
3	44.7	20.2	44.7
4	52.5	23.7	52.5
5	16.8	8.4	4.2
6	13.6	4.5	2.3
7	12.0	9.6	6.0
8	8.5	8.9	5.1

*Post-removal conception rates*

Post-removal conception rates among the ten women who had the implants removed due to planned pregnancy are shown in Table 6. Fifty percent of these women conceived within three months of removal of the implants. The rate was 70% by six months and 90% by the end of one year. In fact, the only woman who had not conceived at one year post-removal was noted to have decided against planned pregnancy and was now using the condom as a method of contraception.

Moreover, it is interesting to note that all nine women have had full-term, normal vaginal deliveries. There has been no untoward incidence of ectopic pregnancy, spontaneous abortion, stillbirth or congenital malformation.

**Table 6** Rates of planned pregnancy by time after removal of Norplant implants in Singapore acceptors

<i>Months after removal</i>	<i>Rate of planned pregnancy (%)</i>
3	50.0
6	70.0
12	90.0

### Discussion

The findings presented in this two-year experience with Norplant subdermal implants suggest that it is a highly effective, safe, and acceptable method among Singapore women. The continuation rate of 79.0% after two years with no pregnancies is comparable with other international studies [2-7].

Furthermore, as demonstrated in other international studies [8-14], disruption of menstrual rhythm, particularly increased bleeding, appears to be the main drawback of the method in the early months of use. The data presented here confirm this, as 47.6% of the removals in the first two years were due to menstrual disturbances. Of the 10 removals due to menstrual disturbances, only one was due to prolonged amenorrhea. Medical problems unrelated to menstruation were few and generally minor [15]. Only one woman had her implants removed due to weight loss, and this was not related to any well-defined disease.

A number of studies now attest to rapidity of conception among former implant users seeking pregnancy. Of patients having Norplant removed for planned pregnancy, 40% had become pregnant by three months, 76% by one year, and 90% by two years [9]. The post-removal conception rate of 90% at one year in this study is comparable to these studies and similar to normal rates of fecundity and the rates for former users of IUD and Depo-Provera [16,17].

### Conclusion

The initial findings of Norplant are encouraging and indicate that the implants are acceptable to Singapore women. Demonstrations of their effectiveness, acceptability, reversibility and comparative safety have convinced many that implants are now the first new major method of contraception to enter family planning programs in the last 15 years. How high the wave of implant acceptance will rise and how forceful it will be must yet be determined. Constraints in terms of costs, physician time, production capacity, and distribution may check potential enthusiasm. It is evident today, however, that Norplant contraceptives will be in strong demand, wherever the current mixture of available contraceptives provide less effective, convenient and satisfactory a mode of reversible contraception [18].

### Acknowledgements

This study was supported by a grant from Family Health International. We are grateful to the medical and nursing staff of Fertility Control Clinic, National University Hospital, for their invaluable help. Finally, we would like to thank Miss Prema for her secretarial assistance in preparing these manuscripts and the Norplant acceptors for their co-operation.

### References

1. Singh, K., Viegas, O. and Ratnam, S.S. (1988). Norplant contraceptive subdermal implants: one year experience in Singapore. *Contraception*, 37, 457-469
2. Lopez, G., Rodriguez, A., Rengifo, J. and Sivin, I. (1985). Two-year prospective study in Colombia of Norplant implants. *Obstet. Gynecol.*, 68, 204-208
3. Basnayake, S., Thapa, S. and Balogh, S.A. (1988). Evaluation of safety, efficacy, and acceptability of Norplant implants in Sri Lanka. *Stud. Fam. Plan.*, 19, 39-48
4. Salah, M., Ahmed, A.G.M., Abo-Eloyoum, M. and Shaabhan, M.M. (1987). Five-year experience with Norplant implants in Assiut, Egypt. *Contraception*, 35, 543-550
5. Affandi, B., Santoso, S.S.I., Djajadilaga, Hdisaputra, W., Moelock, F.A., Prihartono, J., Lubis, F. and Samil, R.S. (1987). Five year experience with Norplant. *Contraception*, 36, 417-428
6. Sayena, B. (1986). Evaluation of Norplant system. In: *Proceedings of the 12th World Congress on Fertility and Sterility, Singapore*, October 1986, Volume 6, S.S. Ratnam, E.S. Teoh, S.M. Lim, eds. Parthenon Publishing Group, London
7. Gu, S.J., Yuan, D.Y., Zhong, L.D. et al. (1987). Evaluation of the Norplant subdermal contraceptive system - China. In: *Proceedings of the Pre-Congress Seminar of the XI AOFORG Congress, Bangkok, Thailand*
8. Satayapan, S., Kanchanasinith, K. and Varakamin, S. (1983). Perceptions and acceptability of Norplant implants in Thailand. *Stud. Fam. Plan.*, 14, 170-176
9. Sivin, J., Diaz, S., Holma, P., San Chez, F.A. and Robertson, N.A. (1983). A four-year clinical study of Norplant implants. *Stud. Fam. Plan.*, 14, 184-187
10. Lubis, F., Prihartono, I., Agoestina, T., Affandi, B. and Sutedi, H. (1983). A one-year experience with Norplant implants in Indonesia. *Stud. Fam. Plan.*, 14, 181-184
11. International Committee for Contraception Research of the Population Council. (1980). Norplant: reversible implant contraception. *Stud. Fam. Plan.*, 14, 163-169
12. Shaaban, M.M., Salah, M., Zar Zaw, A. and Abdullah, S.A. (1980). A prospective study of Norplant implants and the TCu 380 Ag IUD in Egypt. *Stud. Fam. Plan.*, 14, 163-169
13. Diaz, S. (1979). A three-year clinical trial with levonorgestrel silastic implants. *Contraception*, 19, 557-573
14. Singh, K., Viegas, O. and Ratnam, S.S. (1986). Non-biodegradable subdermal levonorgestrel implants (Norplant): preliminary experience in Singapore. *Singapore J. Obstet. Gynaecol.*, 17, 27-32
15. International Committee for Contraception Research (ICCR). (1978). Contraception with long-acting implants. An effective and acceptable modality in international clinical trials. *Contraception*, 18, 315-333
16. Diaz, S., Pavez, M., Cardenas, H. and Croxatto, H.B. (1987). Recovery of fertility and outcome of planned pregnancies after the removal of Norplant subdermal implants contraceptives. *Contraception*, 36, 203-209
17. Affandi, B., Santoso, S.S.I., Djajadilaga, Hdisaputra, W., Moelock, F.A., Prihartono, J., Lubis, F., Samil, R.S. and Saleh, K.R. (1987). Pregnancy after removal of Norplant implants contraceptives. *Contraception*, 36, 203-209
18. Sivin, I. (1988). International experience with Norplant and Norplant-2 contraceptives. *Stud. Fam. Plan.*, 19, 81-94

MS received 18 Mar. 89.

Accepted for publication 21 Apr. 89.

**Resumé**

Les implants contraceptifs Norplant sont des implants Silastic contenant du lévonorgestrel. Cette étude résume nos deux années d'expérience relative à 100 femmes de Singapour qui avaient accepté d'utiliser des implants Norplant. Aucune grossesse n'a été signalée au cours des deux premières années d'utilisation. Vingt implants ont été retirés au cours de cette période, essentiellement pour deux raisons: le désir d'une grossesse planifiée et le dérèglement du cycle menstruel. Le taux de poursuite à la fin de ces deux années s'élevait à 79%. Le pourcentage de grossesses après le retrait chez les femmes désirant une maternité planifiée a atteint 90% à la fin de la première année. Il semble donc que le méthode Norplant offre un mode de contraception extrêmement efficace, acceptable, réversible et sans danger.

**Resumen**

Los implantes anticonceptivos Norplant son implantes Silastic que contienen levonorgestrel. En este estudio se describe nuestra experiencia de dos años con 100 mujeres de Singapur que habían aceptado implantes Norplant. No se registraron embarazos durante los primeros dos años de empleo. El deseo de un embarazo planificado y la perturbación del ritmo menstrual fueron las dos razones principales por las cuales se retiraron veinte implantes en el curso de dicho período. La tasa de continuación al cabo de dos años fue del 79%. La tasa de concepción tras el retiro del implante en las mujeres que deseaban un embarazo planificado fue del 90% al cabo de un año. En consecuencia, parece que el sistema Norplant ofrece un método anticonceptivo de gran eficacia, aceptable, reversible y sin peligro.