DEPO-MEDROXY PROGESTERONE ACETATE AS AN IMMEDIATE POST-PARTUM INJECTABLE CONTRACEPTIVE

By

FOUAD HEFNAWI, ZAKARIA EL SHEIKHA

FAROUK HASSEEB

Obstetrics & Gynaecology Department, Al Azhar University

and

FATMA ABDIN

Pathology Department, Al Azhar University

and

HAYAT ABDEL WAHED

Histology Department, Cairo University

A post-partum family planning programme offers a unique opportunity to reach women in any country in a systematic manner. The use of the event of childbirth to identify the most fertile women is specially important in developing countries where facilities for collecting data are limited.

Teitze pointed out that half of all patients will conceive within three months after their first post-partum menstrual cycle, and 80 per cent will be pregnant again within one year. Therefore, in absence of contraception information for delaying a second pregnancy, conception is likely to occur again after the first ovulation. This possibly occurs within six weeks when the child is not nursed, or after a somewhat longer but undependable time, in the presence of lactation. In any case there may be little time for delayed decision. The immediate post-partum seems an appropriate time for birth control, because we are dealing with an available target, who is already motivated.

A long acting Progestogen as an injectable contraceptive is highly desirable for developing countries, due to its simplicity of schedule of administration.

The use of Medroxy Progesterone Acetate (M. P. A.), a long acting progestogen, as an injectable contraceptive in the immediate post-partum period seems to be promising ; being purely progestational agent, its effect on lactation would be minimal. However, it has been proved by Hefnawi et al. in 1970 that this drug has no adverse effects on milk production in post-partum women, either quantitatively or qualitatively.

We should search for any adverse effects of Medroxy Progesterone Acetate (MPA), since this drug, once injected, cannot be rapidly withdrawn. As the genital organs are target for the action of this drug, the aim of the present study was to evaluate the effect of Medroxy Progesterone Acetate 400 mgm. given twice yearly on the menstrual pattern, endometrium, and vaginal cytology, in post- partum women. Side effects were reported as well as the efficacy of the drug as a post- partum contraceptive.

MATERIAL AND METHODS

This work started in December, 1968, and was conducted during the immediate post-partum period on 68 women delivered at Al-Azhar University Hospital, Cairo. Their ages, ranged from 19 to 42 years (Table 1); their parity ranged from 1 to 10 (Table 2), and the number of pregnancies ranged from 1 to 18 (Table 3). They were given the drug (MPA 400 mgm.) by deep intramuscular injection in the gluteal region. The first dose was given within 24 hours post-partum and was repeated after six months.

TABLE 1

Age Groups of Medroxy Progesterone Acetate (MPA) Acceptors

Age Group	Up to 20 years	21-25 years	26-30 years	31-35 years	36-40 years	Above 40 years
% of Cases	8.3	16.2	26.5	22.0	23.6	2.9

TABLE 2

Parity of Medroxy Progesterone Acetate Acceptors

Parity	1	2-4	5-7	8-10
% of Cases	7.4	48.5	30.9	13.2

TABLE 3

Total Number of Pregnancies in Medroxy Progesterone Acetate Acceptors

Total No. of Pregnancies	1	2-4	5-7	8-10	11-13	14-16	17-18
% of Cases	2.94	22.1	27.9	23.5	16.2	4.4	2.94

Contraception was practised by 32.3 per cent of cases prior to the last pregnancy. Pills or intra-uterine devices were the main methods used. They were stopped due to their side effects.

The indications for the present contraception are presented in (Table 4). A large family size and low income were the main motives to join the trial.

TABLE 4

Indications for Contraception in the Present Study

Indication for Contraception	% of Cases
Family Spacing	7.4
Low Income	13.2
Low Income + Large Family	79.4

A thorough clinical history was taken from all participants. Complete general examination, including heart, chest, breasts and recording the blood pressure was done. Abdominal and pelvic examinations were also done to exclude any abnormality. The participants were re-examined and interviewed one month after delivery (after the first injection), then every other month for a year. During each visit, complete information about menstrual patterns and the condition of lactation were obtained. They were also asked about side effects that followed the injection of the drug and were not present beforehand, especially dizziness, nausea, headache, general weakness, bloatedness, bleeding or spotting, or any other complaints. A thorough physical examination, including examination of the breasts, was done. Pelvic examination and weight recording were also done.

Endometrial biopsies were taken by Sharman's biopsy curette at 1, 3, 5, 7, 9, 11 and 12 months from the first injection (from delivery).

Vaginal smears from the upper third of the lateral vaginal wall were taken one month after the first injection, and repeated weekly every other month for one year.

Cervical smears were taken every two months for one year.

The endometrial biopsies were prepared and stained by haematoxylin and eosin-stain. The vaginal and cervical smears were stained by Papanicolaou's stain.

RESULTS

Each item of the results will be discussed separately, and then a general comment will be presented.

I.—Menstrual Pattern

Excluding the first post-partum month, in which minimal uterine bleeding or spotting are expected as a part of the puerperal lochia, persistent spotting (spotting every day), irregular spotting (spotting + 15 days/month), or occasional spotting (+ 5 days/month) was reported till the end of the second month in almost all acceptors. (By spotting is meant bloody discharge which did not require a sanitary napkin).

Amenorrhoea was achieved by the third month in 60.2 per cent of cases. Its incidence gradually increased to reach 87.5 per cent by the end of the follow-up year, as seen in (Table 5).

TABLE 5

Menstrual Patterns with Medroxy Progesterone Acetate (44 mgm./6 months)

Menstrual Pattern		Months after delivery						
		2	3	5	7	9	11	12
Amenorrhoeic	%	—	60.2	74.0	90.0	74.0	86.7	87.5
Non-Amenorrhoeic	%	100	39.8	26.0	10.0	26.0	13.3	12.5

Minimal but persistent bleeding was complained of by a single woman during the first three months of medication (first three months after delivery). The patient was given iron and tonics, and these made the bleeding tolerable by the patient.

The incidence of spotting gradually decreased, and with the exception of 8 per cent of cases who suffered from irregular spotting (spotting for 15 days/month) in the 9th month, occasional spotting (spotting for + 5 days/month) was the only type of bleeding met with after the 3rd month (Table 6).

TABLE 6

Analysis of Non-Amenorrhoeic Cases with Medroxy Progesterone Acetate

Type of Bleeding	%	Months after delivery					
	2	3	5	7	9	11	12
Bleeding	1.6	1.6	—	—	—	—	—
Every-day Spotting	79.4	14.4	—	—	—	—	—
Irregular Spotting *	19.0	12.8	—	—	8.0	—	—
Occasional Spotting **	—	11.0	26.0	10.0	18.0	13.3	12.5
Total Non-Amenorrhoeic Cases	100.0	39.8	26.0	10.0	26.0	13.3	12.5

* = Spotting on and off from ± 15 days/month.
** = Spotting for less than 5 days/month.

Discussion :

It was shown by Zanartu (1965) and by Soichet in 1969 that in non-puerperal women, the drug caused complete disorganization of the menstrual pattern, with long periods of amenorrhoea, irregular uterine bleeding or spotting. However, the bleeding was seldom heavy. Mishell (et al) in 1968 administered the drug in a dose of 150 mgm. every three months to 100 post-partum women. They encountered bleeding or spotting for more than 21 days in the first month, and it decreased thereafter. They encountered bleeding for more than 7 days in 35.7 per cent of cases in the fourth post-partum month (the first month after the second injection).

In the present study, while all participants reported spotting till the end of the second month post-partum (except one case who reported bleeding) the incidence of amenorrhoea by the third month was

60.2 per cent which gradually increased to reach 90 per cent at the 7th month (the first month after the second injection) and 87.5 per cent by the 12th month.

The lower incidence of spotting in the present study during the 7th month (the first month after the second injection) may be related to higher doses used.

Spotting and Amenorrhoea as a Side-Effect in the Post-Partum Period :

Minimal bleeding and spotting during the first month post-partum was considered by most of the women as a part of the puerperal lochia. Most of the participants tolerated spotting that occurred later on, as they considered that the contraceptive advantages far out-weighed the inconvenience.

Although amenorrhoea is an undesirable effect, it did not worry post-partum women since it is expected and considered physiological during this period, especially in the presence of lactation.

Whether the lactational amenorrhoea is physiological or pathological is a matter of discussion. While Janny (1945) and Melkani (1960) considered all cases of lactational amenorrhoea as physiological with exceptions, Beclere (1943) and Pundel (1951) considered it pathological if it exceeds 3 and 4 months respectively. It seems that lactational amenorrhoea is physiological with exceptions as evidenced by the high fertility in Egypt in spite of the prolonged period of lactational amenorrhoea, and it was shown by El Minawi (1963) that ovulation occurred in his cases after 18 months of lactational amenorrhoea.

II.—Lactation

In all participants, breast feeding continued till the end of the follow-up year, except those who lost their babies (6 cases) due to gastroenteritis and chest infections.

Discussion :

Medroxy Progesterone Acetate, being a purely progestational agent, its effect on lactation would be minimal, especially as its metabolites have no oestrogenic effect. However, it is as emphasized by Hafnawi et al. in 1970, that the drug has no adverse effect on lactation either quantitatively or qualitatively.

III.—Breasts

The breasts did not reveal any soreness or nodularities.

Discussion :

It was found by experimental work that the drug caused nodularity of the breasts of rodents, but since no abnormality could be detected in humans it appears that is due to species difference.

IV.—Side-Effects of the Drug

Side effects other than spotting and amenorrhoea were minimal 14.7 per cent of cases complained of a transient sense of fatigue for 3 to 5 days after the injection.

Two cases showed an increase in weight above 3 kilogrammes, otherwise there was no appreciable change in weight.

No other side effects were reported.

Discussion :

The drug has minimal side effects when used in the post-partum period since early spotting may be considered as a part of the puerperal lochia, and amenorrhoea as a physiological event.

V.—Drop-Outs

The drop-out rate for the second injection was 26.4 per cent of total cases. The causes for that are presented in (Table 7).

TABLE 7

Drop-Outs for the Second Injection

Reason	% of Total Drop-Outs
Planned Pregnancy	22.22
Travelling	11.11
Spotting	16.67
Discomfort from repeated biopsies and smears	33.33
Difficulties in maintaining the prolonged follow-up	16.67
Total Drop-Out %	100

Discussion :

The acceptability rate for the drug was high. It perhaps would be higher if repeat biopsies were not taken from the participants.

VI.—Effectiveness

The drug was effective as a post-partum contraceptive in 100 per cent of cases.

Discussion :

Zanartu in 1968 reported a «drug failure» rate of 1.13 per 100 — women-year, when using the drug in doses ranging from 250 to 1000 mgm. every six months in non-puerperal women. Zelenik (1969) administered the drug in a dose of 150 mgm. every three months in non-puerperal women and reported a failure rate of 0.49 per 100-women-year, mostly by the end of the third month or the beginning of the fourth month, which may indicate that the dose was insufficient.

However, when the drug was used in a dose of 150 mgm./3 months by Mishell et al. and a dose of 400 mgm./6 months in this series, no pregnancies occurred during the follow-up year. This means that contraceptive efficacy of the drug is very high, especially so in the post-partum period.

VII.—Effect on the Endometrium

A total of 361 endometrial biopsies were attempted. Of these, 33 specimens were insufficient for detailed description. The endometrial pictures are presented chronologically as follows :

(*a*) Biopsies taken one month after the first injection (63 biopsies) showed : moderate endometrial thickness, with numerous glands per lower power field. These were of moderate size, lined by columnar epithelium, showing weak secretory activity. The stroma showed minimal oedema, stromal haemorrhages, and numerous thin walled superficial blood vessels.

(*b*) Biopsies taken three months after the first injection (57 biopsies) showed : moderate endometrial thickness, with a decrease in number of glands per lower power field, which did not show any secretory activity.

— Cystic dilatation of some glands was found in 12.3 per cent of specimens, but without cellular hyperplasia or mitosis.

— Stromal oedema increased, stromal haemorrhages were present numerous thin walled blood vessels were seen near the surface.

(*c*) Biopsies taken five months after the first injection (50 biopsies) showed : further decrease in the endometrial thickness and number of glands per lower power field, with no evidence of secretion. Cystic dilatation of some glands was noticed in 4 per cent of specimens. The stromal oedema increased stromal haemorrhages were minimal. The superficial blood vessels decreased in number and in diameter.

(*d*) Endometrial biopsies (46 biopsies) obtained 7 months after the first injection (one month after the second injection) showed further decrease in endometrial thickness, few small glands with no evidence of secretion. The stroma showed patchy pseudo-decidual reaction. The blood vessels mainly something is missing here deep.

(*e*) The regressive changes in the endometrium reached its maximum at the 9th month and the endometrial picture was the same after 9, 11, and 12 months showing diffuse pseudo-decidual reaction and minimal glandular tissue.

Discussion :

The endometrium was subjected, very early in the puerperium ; to a uniform and prolonged effect of a puraly progestational agent, without cyclic variation or interruption and without any added oestrogen. This resulted in what is called «steroidal endometrium», to which the ordinary descriptive terms, proliferative or secretory, are not justifiable. So, in a «steroidal endometrium» every element must be thoroughly observed and described.

Zanartu in 1966 noted regressive changes in the endometrium under the effect of the drug in non-puerperal women. Mishell et al. in 1968 did not find any secretory activity in endometrium when they injected the drug in a dose of 150 mgm. every three months and they interpreted the endometrium as being minimally proliferative, quiescent, or atrophic. They were not able to detect secretory activity in the endometrium because they started to obtain biopsies after six weeks post- partum and repeated that every three months.

In the present study secretory endometrium was detected one month after the first injection which means that, when the drug is given to the non-puerperal women, the endometrial changes will not share with its maximum power in the contraceptive effect of the drug, in the first month of medication.

Although the endometrium showed a gradual decrease in thickness and in number of glands, the discrepancy in response of the epithelium and stroma, as a result of continuous prolonged progestational effect was very obvious, seven months after medication. While the glands were few in number and small in size without any secretory activity, the stroma showed patchy pseudo- decidual reaction. Two months later, though the endometrial thickness showed further diminution, the pseudo-decidual reaction of the stroma became diffuse and its amount was more than seen in typical atrophic endometrium, with a decrease in both the strome and epithelial components.

No abnormal stromal cells were encountered throughout the period of the follow-up, while abnormal large and pale stromal cells were reported by Dockerty et al. (1959) in patients using combined oral contraceptive pills.

Correlation between Endometrial Findings and Menstrual Patterns :

Lee in 1969, in a series of 14 patients, found a relationship between the decreased incidence of spotting and the incidence of cystic dilatation in biopsies taken six months after medication. After 9 and 12 months, he reported minimal spotting in cases from whom he failed to obtain biopsies. However, he did not see the endometrial picture in the first 6 months, which is the period of maximal incidence of spotting.

However, in the present study, the high incidence of spotting that occurred early in medication could be related, among other factors, to the numerous thin-walled stromal superficial blood vessels. The gradual increase in the incidence of amenorrhoea could be related to the gradual decrease in thickness and vascularity of the endometrium.

The Relation between the Endometrial Changes and the Contraceptive Effect of the Drug :

For embedding to occur, a suitable endometrium in the secretory stage with abundance of glycogen and loose oedematous stroma and containing numerous blood vessels has to be present, coinciding with

the arrival of the blastocyst. For such endometrial features to occur, a delicate balance between oestrogen and progesterone must exist (Parkes, 1965). According to Brews (1963) there is a mutual interdependence between the trophoblasts and the sensitized endometrium. This has been emphasized by Hafez and Pincus in 1965.

The endometrial picture under the effect of Medroxy Progesterone Acetate showed weak secretory activity in biopsies taken one month after the first injection (after delivery), and it rapidly became exhausted and no evidence of secretion was detected later on.

This shows that, by the time ovulation is about to occur, if it occurs (under the effect of the drug), the endometrium will be unsuitable for nidation. Also the decreased glandular activity produced by the drug may interfere with the proper nourishment of the blastocyst prior to implantation.

VIII.—Cytological Findings

Repeated vaginal smears (1200) showed a dominant progestational effect with a mid-zonal shift of the «Maturation Index» and no cyclic variation pointing to anovulation.

Cervical and vaginal smears did not reveal cellular atypia under the effect of the drug.

Discussion :

The cytological findings showed that the drug is safe. Both endometrial findings and cytological findings denoted dominant progestational effect and are suggestive of anovulation.

COMMENT

An ideal contraceptive for the post-partum period should not interfere with the physiological function of the breats, and proper breast feeding.

Pills need continuous motivation for taking them daily ; also some side effects including inhibition of lactation make them unsuitable. This is especially true if used in developing countries where lactation is an important economic factor and is the only method of adequately nourishing the child.

Although intra-uterine devices remove the need for the patient's responsibility, their application to post-partum women is not suitable. Their rate of expulsion in the puerperium was seen to be remarkably high, amounting to 40 per cent (Phatok and Meena Bhatra, 1968). Most perforations have been reported to occur when the device is inserted 5 to 6 weeks post-partum (Esposito, 1966 ; Ledger, 1966 ; Tietze, 1966). These, together with the liability of haemorrhage and infections, make the devices less suitable as a post-partum contraceptive.

Depot Medroxy Progesterone Acetate, being an aqueous suspension of micro crystals, is slowly absorbed from the injection site and so it has a prolonged effect, hence its use as a long acting contraceptive. It has no adverse effect on lactation (Hefnawi et al., 1970), and its side effects are annoying rather than serious and could be easily accepted and tolerated by puerperal and lactating mothers. Its use as a post-partum contraceptive in developing countries is promising.

Effectiveness of Medroxy Progesterone Acetate as Contraceptive :

The efficacy of the drug is very high. While Zanartu in 1968 reported a drug failure rate of 1.13 per 100-women-year in non-puerperal women, Zelenik in 1969 reported a failure rate of 0.49 per 100-women-year, Soichet in 1969 reported 100 per cent efficacy. When used by Mishell et al. in 1968 and by the writer, the drug was 100 per cent effective.

Mode of Action of Medroxy Progesterone Acetate :

The mode of action is thought to be through :

1. Inhibition of ovulation.
2. Its effect on the endometrium.
3. Change in the cervical mucus.
4. May be through its effect on the tubes.

Kupperman and Epstein (1962) and Laron et al. (1963) reported that the drug suppresses gonadotrophin secretion in human beings. This was emphasized by Mishell (1967) who found that the drug interfered with the release of luteinzing hormone, when used in a dose of 150 mgm. every three months. In the writer's study, the high effectiveness, the regressive changes in the endometrium, the absence of cyclic variation in vaginal cytology, and the high incidence of amenorrhoea pointed to anovulation.

The marked regressive changes that occurred in the endometrium in this study as well as shown by Zanartu (1966), Mishell et al. (1968) and Lee (1969) may interfere with nidation as discussed above.

The cervical mucus during therapy became thick and tenacious and it was shown by Zanartu in 1966 that the tolerance to sperm was reduced to zero.

Its action at tubal level, however, was regarded by Zanartu (1966) to be due to its effect on the cells of the endosalpinx. He noticed that the cells were low and apparently inactive in respect to secretion.

Side-Effects :

Apart from spotting in early medication and amenorrhoea later on, no major side effects were reported by the participants in the writer's series. Only 14.7 per cent suffered from a sense of general weakness for a period of 3 to 5 days after injection. However, the acceptability rate was high. No appreciable change in weight occurred. Mishell et al., using the drug in a dose of 150 mgm./three months, reported similar findings as regards weight. They did not report any serious side effects.

Effects on Breasts and Lactation :

Though the drug causes some nodularity in the breasts of rats, reported examination of the breasts in this study did not reveal any abnormality during the whole period of follow-up.

Hefnawi et al. in 1970, after detailed biochemical study on lactation under the effect of the drug, reported an increase in the quantity of milk yield, and in the quantity of milk proteins, as compared with controls. The lactating child has shown no interference with the expected growth and weight progress.

Safety :

No adverse effects were observed on the participants, vaginal and cervical cytology did not reveal any cellular atypia, under effect of the drug.

SUMMARY

For mass population control, especially in developing countries, Depot Medroxy Progesterone Acetate is an important post-partum contraceptive measure. Its use in the immediate post-partum period nullifies its main side effects (spotting early in medication, followed

by amenorrhoea). Most women in developing countries regard spotting in the first month post-partum as normal, and accept amenorrhoea as a physiological event with lactation.

It main use would be for one year or so during lactation, thereafter the patient would use another form of contraception.

It is safe and its side effects are annoying rather than serious.

REFERENCES

BECLERE, C. and SIMONNET, H. : «L'amonorrhee survenant l'accouchment. Son treatment part les hormones gonadotropes».
Gyn. et Obst. 43 : 349, 1943 (quoted by El-Minawi, M. F., M.Ch. Thesis, «Histological and Cytological Changes in Lactation», 1963).

BREWS, A. : «Holland and Brews Manual of Obstetrics, 12th Ed. J. & A. Churchill, Ltd., Publishers, London, 1963.

DOKERTY, M. B. ; SMITH, R. A. and SYMMONDS, R. E. : «Proc. Mayo Clin. 34 : 321, 1959, (Quoted from Pincus, 1965).

ESPOSITO, J. M. ; «Perforation of the Uterus, secondary to Insertion of IUCD». Obst. & Gyn., 28 : 799, 1966.

HAFEZ, E. S. E. and PINCUS, G. : «Inhibition of Implantation by Deciduoma Formation in the Rabbit».
Fertil. & Steril., 7 : 422, 1965.

HEFNAWI, F. and EL-SHEIKHA, Z. : «Contraception with long acting injection progestogen in the immediate post-partum period». Presented to the Fourth Symposium on Family Planning, Dar El Hekma, Cairo, 25-27 October, 1969.

HEFNAWI, F. ; FAWZI, G. ; BADRAWI, M. H. ; ABDEL KADER, M. M. and BAHGAT, M. R. : «Attempts to select a suitable hormonal contraceptive during lactation».
Presented to the 6th World Congress of Obstetrics and Gynecology, New York, April, 1970.

JANNEY, D. C. : «Medical Gynaecology, Philadelphia», Saunders 1945.

KUPPERMAN, H. S. and EPSTEIN, J. A. : «Medroxyprogesterone Acetate in Treatment of Constitutional Sexual Precocity».
J. Clin. Endo. and Metab. 456-458. April, 1962.

LARON, Z. ; RUMNY, G. and RAT, L. et al. : «Effect of 17 a-hydroxy-6 a-Methyl Progesterone Acetate on Urinary Gonadotrophin and Oestrogen in Man».
Acta Endocr. 44 : 75-80, September, 1963.

LEDGER, W. J. and WILLSON, J. R. : «Intra uterine Contraceptive Devices : The Recognition and Management of Uterine Perforations». Obstet. & Gyn., 28 : 806, 1966.

LEE, R. A. : «Contraceptive and Endometrial Effect of Medroxy Progesterone Acetate».
Am. J. Obstet. Gynéc., May 1, 1969.

MALKANI and MIRCHANDANI of New DELHI, P. K. : «Ovulation during Lactation as determined by Endometrial Biopsy». J. Obstet. Gynaec., India. 11/3, 121-127, 1960.

EL-MINAWI, M. F. : «Histological and Cytological Changes in Lactation» M.Ch. Thesis, Cairo, U. A. R. 1963.

MISHELL, D. R. ; EL-HABASHY, M. A. ; GOOD, R. G. and MOYER, L. D. : «Contraception with an injectable progestin. A tudy on Post-partum Women». Am. J. Obstet. Gynec., 101 : 8, 1968.

PARKES, A. S. : «Biological Aspects of the Control of Human Fertility». Practitioner, 194, 455, 1965.

PHATOK, L. V. ; MEENA BHATRA : «Observations on Expulsion of the IUCD in Puerperal and non-Puerperal Insertions». Am. J. Obstet. Gynec., 101, 6 : 773, 1968.

PUNDEL and FRED VAN MEENSEL : «Gestation et Cytologie Vaginale». XII, Partie, 1951.

SOICHET, S. : «Depot Provera (Medroxy Progesterone Acetate as a Female Contraceptive Agent). «International Journal of Fertility Jan. — Mar. 14 : 33, 1969.

TIETZE, C. : «Contraception with Intra Uterine Contraceptive Devices». Am. J. Obstet. Gynec., 96 : 1043, 1966.

ZANARTU, J. and ROSEMBERG, D. : «The Effect of Cyclic Oestrogens, sequential or combined oestrogen and progesterone and long acting progestagen therapy in human ovaries». Report to the VIth Pan-American Endocrine Meeting, Mexico City, October 1965.

ZANARTU, J. : «Effect of Natural and Synthetic Sex Steroids on Cervical Mucus, Penetration and Ascent of Spermatozoa». Report to the Vth World Fertility and Sterility Congress, Stockholm.

ZANARTU, J. ; RICE-WRAY, E. and GOLDZIEHER, J. W. : «Fertility Control with long-acting steroids». Obstetrics and Gynaecology 28 : 513, 1966.

ZELENIK, J. S. : «Injectable Contraceptive in Northern Thailand». The Official Journal of Public Health Assoc. of Pakistan, 2 : 20, No. 1, Jan. — Mar. 1969.