Technical Reports

A review

Steroid Contraception and its Effects on Lactation are a Public Health Dilemma

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"I SWEAR by Apollo the physician . . . I will prescribe regimen for the good of my patients according to my ability and my judgment and never do harm to anyone. . . ."—Hippocrates

Family planning is taking its place as one of the leading priorities of many of the world's peoples. Steroid contraceptives are becoming a cornerstone in successful family planning programs. Yet, in some areas of the world, steroid contraceptives may become a double-edged sword.

"Breast feeding is one of the most effective ways of overcoming factors related to lack of resources, such as infection and poor nutrition. Since these factors are of such importance, a significant increase in the practice of breast feeding would surely lead to a reduction in infant mortality" (*1*). Conversely, a decrease in the practice of breast feeding would lead to an increase in infant mortality. Kwashiorkor means "first-second" according to some sources or "the disease the child gets when the next baby is born" (*2*). In other words, protein malnutrition comes about only after the mother stops breast feeding her infant. A frequent reason for the discontinuation of breast feeding is the next pregnancy. According to Semm (*3*), in only about 50 percent of lactating women is pregnancy delayed until after the cessation of breast feeding. Kwashiorkor is a major cause of infant morbidity in many developing countries. Therefore, in these countries, the length of time that a mother successfully breast feeds her infant has a profound influence on the future of that child.

It might well be argued that increasing the time between pregnancies would increase the mean lactating time for the receiving infant. In many areas this increase would be advantageous to the infant's health. To obtain more time would require the use of a contraceptive. If, however, this contraceptive measure had as one side effect a decrease in the mean period of lactation or a detrimental effect on the nutritive value of breast milk, then it would lose much of its positive value. In this regard, steroid contraceptives have come under heavy attack.

Results of Studies

Many studies of animals have been done to determine the effect of steroid contraception on lactation. These studies as predictors of human response must, however, be suspect, as Joshi and Rao (*4*) showed wide variation in response to the same drug in three animal species. They gave 5.0 mg norethynodrel plus 75μg mestranol (see box) to the mouse, the rat, and the rabbit in a high and a low dosage form. The lower dose was

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two times the human dose on a milligram-for-kilogram basis, which also happened to be the minimal effective dose for contraception in these animals. The higher dose was 20 times the human dose on a milligram-for-kilogram basis. The litter numbers were limited to six each in the mouse and rat and to three in the rabbit.

The growth curve of the litter was used as an index of efficiency for lactation. In the rat, both the low and the high dosages resulted in a 10 to 20 percent inhibition in the growth rate of the young as compared with the controls. In the mouse, neither dosage affected lactation. In the rabbit, a slight increase in growth rate was noted in the young.

Kamal and associates (*5*) summarized some literature concerning human experience. They quoted Satterthwaite and Gamble as observing that when norethynodrel was given in either 5 mg or 10 mg tablets, a markedly deleterious effect on the production of milk occurred in the first and second cycles. They quoted Chinnatamby as finding that 2.5 mg norethynodrel plus 100 μg mestranol was most depressant of lactation in women with a history of short lactation. They also quoted Kubba, noting that when 2.5 mg lynestrenol plus 75 μg mestranol was used, a marked decrease occurred in lactation, whereas when 2.5 to 5.0 mg lynestrenol was used continuously for 6 months, lactation was not affected.

Kamal and associates (*5*) discussed a Hayden finding: that when 2.5 mg norethynodrel plus 100 μg mestranol was given to 30 women, while 30 controls received a placebo plus a mechanical intrauterine device (IUD) for contraception, the length of lactation was not adversely affected if the history of success in lactation was considered. They said Rogers and associates had noted that inhibition of lactation occurred only when the oral preparation contained estrogen and that milk yield actually increased when an IUD was used.

Rice-Wray and associates (*6*), in an uncontrolled study, found that 10 mg norethindrone plus 60 μg mestranol resulted in decreased or totally inhibited lactation in 32.5 percent of the women treated.

Ferin and associates (*7*) found that 2.5 mg lynestrenol had no effect on lactation as gauged by the infant's weight-curve increases and by the rate of continuing full breast feeding without supplementation by the mother.

Hefnawi (*8*) studied 401 multiparous women. He administered to these women, in six groups,

Steroid contraceptives named in this study

Generic name	*Trade name*
5.0 mg norethynodrel plus 75 μg mestranol	Enovid (5 mg)
2.5 mg norethynodrel plus 100 μg mestranol	Enovid E
2.5 mg lynestrenol plus 75 μg mestranol	Lyndiol (2.5 mg)
5.0 mg lynestrenol plus 150 μg mestranol	Lyndiol
4.0 mg norethisterone acetate plus 50 μg ethinyl estradiol	Anovlar
3.0 mg chlormadinone acetate plus 100 μg mestranol	Aconcen
1.0 mg ethynodiol diacetate plus 100 μg mestranol	Ovulen
10 mg norethindrone plus 60 μg mestranol	Ortho-Novum
150 mg dihydroxyprogesterone acetophenide plus 10 μg estradiol enanthate	Deladroxate

one type each of six different contraceptive pills (5.0 mg lynestrenol plus 150 μg mestranol, 4 mg norethisterone acetate plus 50 μg ethinyl estradiol, 3 mg chlormadinone acetate plus 100 μg mestranol, 1.0 mg ethynodiol diacetate plus 100 μg mestranol, 0.5 mg ethynodiol plus 100 μg mestranol, and 0.25 mg ethynodiol plus 100 μg mestranol). A mild decrease occurred in the total duration of lactation. The study results, however, depended on the mother's word and memory. The amount of milk yielded was not estimated directly, nor was the curve showing the growth of the infant.

Gold (*9*) quoted Kora as showing that, when 62 mothers who had lactated between 4 and 24 weeks took 1.0 mg ethynodiol diacetate plus 100 μg mestranol, lactation was affected negatively in a statistically significant fashion in certain parameters when compared with controls. Infants of the control group mothers received greater amounts of breast milk than infants of the mothers in the treatment group. The amount of milk obtained from the control mothers increased weekly, while the mothers who were medicated produced less milk than they did before receiving the medication. The weekly gain in weight was significantly less for the treatment infants than for the control infants. In this study, however, the control group consisted of 15 mothers who did not receive a pill. The study, therefore, was not blind.

Gold quoted Ibrahim and El-Tawil, who also used 1.0 mg ethynodiol diacetate plus 100 μg mestranol as their test drug. Treatment was given to 32 multiparas and 15 primiparas "as early as possible" after lactation was established—usually within 3 months after delivery. Lactation was adversely affected in the multiparas when com-

pared with their history of lactation. In previous pregnancies 71.5 percent of the multiparas in the study had nursed their infants for more than 3 months, 62 percent for more than 6 months, and 47 percent for more than 1 year. With 1.0 mg ethynodiol diacetate plus 100 μg mestranol, successful lactation stopped after 6 months in 81 percent of the patients. There were no controls in this study.

Miller and Hughes (*10*) conducted a double blind study involving 100 women who had healthy term infants and who expressed the desire to have oral contraception and also to nurse their infants for 3 months. Group 1*a* consisted of 25 women given 1 mg norethindrone plus 80 μg mestranol on the 14th post partum day, then the pill in cycles of 21 days on and 7 days off. Group 1*b* received placebos in the same manner. Groups 2*a* and 2*b* were the same groups as 1*a* and 1*b* except that they started their pills 6 weeks post partum. Lactation was adversely affected in the mothers on medication when compared with the mothers on placebos. Weight gain decreased in the infants of medicated mothers, even when supplements were increased for the infants and their total caloric intake was greater than that of the infants of mothers given a placebo. The decrease in duration of lactation was more pronounced in primiparas when compared with those who had previously achieved successful lactation.

Kamal and associates (*5*) reported a double blind study involving 50 lactating women, 6 to 10 weeks post partum. Ten women were placed in five groups. Group 1 received 2.5 mg lynestrenol plus 75 μg mestranol; group 2 received 1.0 mg lynestrenol plus 100 μg mestranol; group 3 received 0.5 mg lynestrenol alone, daily, continuously; group 4 received a long-acting injectable steroid (150 mg dihydroxyprogesterone acetophenide and 10 mg estradiol enanthate); group 5 received an IUD and a placebo pill.

Groups 1, 2, and 5 received pills for 22 days, followed by 6 days without pills. Group 4 received an injection the 8th day of each 28-day cycle. The results of this study were not significant. Groups 1 and 4 had the most deleterious effect on lactation, while group 3 had the least effect.

Kamal and associates (*11*) also reported another double blind study. Forty women who delivered by cesarian section were separated into four groups and followed over a 12-day period, starting on day 2 post partum. Group 1 received a placebo, group 2 an estrogen (0.1 mg ethinyl estradiol, group 3 a progestogen (0.5 mg lynestrenol), and group 4 a combination of 1 mg lynestrenol plus 100 μg mestranol. Milk production increased in all medicated women, especially those in group 3.

Kaern (*12*) studied 451 mothers who delivered infants at St. Joseph's Hospital in Copenhagen between July and September 1966. This group consisted of all the women, except three, who gave birth at this hospital in the indicated timespan. The three women excluded consisted of one who, it was decided, "should not attempt to breast feed" and two mothers who gave birth to infants weighing less than 2,000 grams. This study, also double blind, consisted of two groups. Group 1 mothers received 1 mg norethisterone plus 50 μg mestranol daily, starting day 1 post partum and continuing until day 8. Group 2 received placebos in a similar manner. The results were studied to determine—

1. Need for supplementary feedings of primiparas and multiparas, separately
2. Weight change between day 2 and day 8 in those infants of mothers who did not require supplementary feedings.

Infants of medicated multiparas required supplementary feedings more frequently than infants of multiparas who received a placebo, significant at the 1 percent level of confidence. The outcome was similar for primiparas but significant only at the 5 percent level. The weight change between day 2 and day 8 of infants who were breast fed only was greater in the placebo group, but only between the 5 and 10 percent level of confidence.

Borglin and Sandholm (*13*) studied lactating women whose infants were admitted to a pediatric ward for various reasons. Milk was expressed from the breasts of these women at regular intervals with an electric breast pump. The women were placed on one of four regimens in a double blind fashion. Group 1 received 2.5 mg lynestrenol plus 75 μg mestranol, group 2 received 0.05 mg ethinyl estradiol, group 3 received 80 μg mestranol, and group 4 received a placebo. The women were instructed to take one tablet daily during the second week only of a 3-week investigation.

Milk was measured in 3-day totals during five different periods. Period one consisted of the 3 days directly before the tablet regimen was started, periods two and three consisted of two 3-day periods while the women were taking the tablets, and periods four and five consisted of

two 3-day periods in the week after the women ceased taking the tablets.

A total of 37 trials were made on 29 women. Women participating in more than one trial had at least 2 weeks between trials. The results showed that women on 2.5 mg lynestrenol plus 75 μg mestranol produced significantly less milk than those on a placebo ($P < 0.01$). Women on ethinyl estradiol also produced less milk than those on a placebo ($P = 0.05$).

Semm (*3*) conducted a double blind study with 100 women, 1 day post partum, who desired to lactate. Fifty women were given 2.5 mg lynestrenol plus 75 μg mestranol daily, and 50 women were given a placebo. Infants were weighed before and after feedings. Mothers and infants remained in the hospital for 10 days. At the end of the 10 days there was no difference in weight gain between the two groups. The mothers were instructed to continue their regimens at home and weigh the infants before and after feedings. At the end of another 3 weeks, still no difference had occurred between the groups.

Semm then studied an additional 70 women in the same fashion, but began the pill regimen at 10 days post partum, so that lactation already had been established. The infants of mothers on 2.5 mg lynestrenol plus 75 μg mestranol gained more weight than those of mothers on a placebo, but the difference was not statistically significant.

Kader and associates (*14*) studied the composition of human milk as affected by steroid contraception. A double blind study was conducted involving lactating mothers who were 6 to 10 weeks post partum. Ten mothers were randomly allocated to five groups. Group 1 received 2.5 mg lynestrenol plus 75 μg mestranol daily for 22 days, followed by no medication for 6 days; group 2 received 1.0 mg lynestrenol plus 100 μg mestranol daily in the same manner as in group 1; group 3 received 0.5 mg lynestrenol daily, continuously; group 4 received 150 mg dihydroxyprogesterone acetophenide, a long-acting injectable steroid, on day 8 of each cycle; and group 5 received an IUD and a placebo in the same cycling as for group 1. Milk proteins, fat sodium, potassium, calcium, and magnesium were all significantly decreased for groups 1 through 4 when compared with group 5, the control group.

Toaff and associates (*15*) studied healthy nursing mothers who qualified as follows:

1. Each had an uncomplicated second to fifth delivery at term
2. The mother was not excessively fat
3. Breast feeding was planned.

The study used random selection and was double blind. A total of 175 mothers were studied. Group 1 consisted of 66 women who received 0.3 mg ethinyl estradiol daily, divided into three equal doses; group 2 consisted of 63 women who received 50 mg 6-alpha-methyl-17-alpha-hydroxyprogesterone acetate per day, divided into three equal doses; group 3 consisted of 46 women who received a placebo in the same manner as groups 1 and 2 received drugs. Treatment was started at 1 to 4 hours post partum and was continued for 5 days. One sample was taken from each mother at the end of the 10 a.m. feeding on the 5th day. Group 1 mothers had an increased protein content in their milk when compared with the control group, significant at the 1 percent level of confidence. Group 2 had a decreased fat and total solids content, but this result was not statistically significant. The yield of milk was not affected.

Karim and associates (*16*) studied the effect of injected progestogen on the lactation of 331 mothers who had delivered normally and who were breast feeding their infants. The study was not blind. Group 1 consisted of 100 women who were followed from the 7th day post partum; they served as controls. Group 2 consisted of 112 women who were subdivided into two groups. Group 2*a* consisted of 57 women who at 42 days post partum received 200 mg norethisterone ethanate by intramuscular injection. This dose was repeated every 84 days. Group 2*b* consisted of 55 women who at 42 days post partum received 150 mg medroxyprogesterone acetate by intramuscular injection. This dose was repeated every 3 months.

Group 3*a* consisted of 68 women who were treated in the same way as group 2*a* except that they received their first injection on the 7th day post partum. Group 3*b* consisted of 51 women who also were treated in the same way as group 2*b* except that they received their first injection on the 7th day post partum. The infants' weights were statistically better ($P < 0.01$) in the treated groups after 3 months. The average amount of milk available every 3 hours was greater in the treated groups after 3 months ($P < 0.05$) and after 4 months ($P < 0.01$). The average milk proteins were decreased in all three groups when compared with standards for milk proteins ($P < 0.05$). This decrease was attributed to the low intake of protein by the mothers. The

average milk fat, lactose, and total solids showed no statistically significant change. Physical examination of the infants at 18 months of age showed no difference among the three groups.

Discussion

I have presented a variety of studies with findings on steroid contraception and its effect on lactation. A number of these studies were controlled and double blind. Yet there is little agreement among their findings. Why? Borglin (*17*) sheds some light on this problem. He studied the effect of 2.5 mg lynestrenol plus 75 μg mestranol and a placebo on lactation in women who did not want (or have) to lactate. He used a double blind technique. Thirty women were randomly allocated to each of two groups. The results follow:

Effect on lactation	*2.5 mg lynestrenol plus 75 μg mestranol*	*Placebo*
Inhibition	21	19
Slight secretion	5	3
Unchanged	4	8
Total	30	30

Lactation in 21 of the 30 women receiving 2.5 mg lynestrenol plus 75 μg mestranol was completely inhibited; they had no engorgement of milk flow. This result is rather impressive until we consider that 19 of 30 women who received a placebo experienced the same effect. What does this mean?

The remainder of this paper is devoted to what I think is at least one possible explanation for the dichotomy in the results of many rather good investigations. I deal mainly with the studies that were controlled and double blind.

At least two major factors seem to determine the effect of steroid contraception on lactation. One is the quantity and quality of progestogens and estrogens in various preparations. The other is the psychological attitude of the patient taking the medication. Borglin (*17*) and Semm (*3*) used the same drug, 2.5 mg lynestrenol plus 75 μg mestranol, but for different stated purposes. Semm used it as a contraceptive, while Borglin used it to inhibit lactation. The drug's effect on lactation was opposite.

These studies actually are not directly comparable, but I believe there is good evidence to indicate that the psychological factor was the dominant one in determining the outcome. What the patient believes the medication will do concerning lactation can be the outstanding factor.

According to Hefnawi (*18*), it is common knowledge, at least in Egypt, that "the pill" inhibits or diminishes lactation. This attitudinal variable could well be the factor that has confounded so many results. A random allocation of patients to various groups should in theory randomize the attitudes of the patients as well. It would be interesting, nonetheless, to obtain an attitudinal profile of the study patients. This profile would be especially important if the numbers studied were small.

In Kaern's study (*12*), the control group infants apparently did better than the infants of medicated mothers. The study involved 451 of 454 consecutive deliveries. It would be hard to believe that, even in Copenhagen, these women were all equally desirous of breast feeding their infants. Perhaps a group consisting of women who were uniformly desirous of breast feeding and who thought the pill they received would not be deleterious to lactation would be able to have a positive psychological attitude that would offset a negative effect from medication.

In at least several studies, one parameter investigated was a comparison of previous periods of lactation with those in the current study. I have seen no results in which the current study does not come in second best by this comparison. It is true that comparison depended on the memory of the mothers and that this could hardly be called an objective measurement. Nonetheless, it seems odd that in no study did the mothers recall a shorter length of lactation after the previous pregnancy even when compared with the controls, who received a placebo.

I believe that this result is significant. Even if the group receiving placebos and the group receiving medication showed no difference, lactation in both groups could have been psychologically affected as compared with a group of women who received nothing. What the mother who is lactating thinks the pill will do may be the crucial factor; therefore, the simple act of giving a placebo may have the same effect on lactation as administering active ingredients.

Public health programs are consequently presented with a dilemma: family planning with its many beneficial aspects, on the one hand, and the possibility of limiting the quality and quantity of breast milk, on the other. What should be done? In areas where breast milk is the major source of

sterile as well as nutritious food, a contraceptive should be selected that apparently has the least inhibiting effect on lactation. In addition, a vigorous attempt should be made to change the attitude of the recipients of this medication in a positive direction, or at least to a neutral position. If this cannot be accomplished, an IUD may well be the preferred method of contraception.

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Although steroid contraceptives may offer significant advantages over the more traditional methods of family planning, they may adversely affect the quality and quantity of breast milk. In some areas of the world, breast milk is the only source of sterile nutritious food for infants. This fact presents a public health dilemma.

The literature offers a number of good studies dealing with the effects of steroid contraceptives on lactation. Some of these studies are controlled and double blind, yet there is little agreement on the findings. Some studies found steroid contraceptives to be detrimental to successful breast feeding, while others found no such effect. Psychological factors may well be responsible for this dichotomy.

Apparently the quantity and quality of progestogens and estrogens in steroid contraceptives can affect lactation to a lesser or greater degree. How a pill or injection will affect lactation, however, can be significantly altered by how the mother believes the pill or injection will affect her lactation. If a mother believes that a medication can adversely affect her lactation, then it is likely that it will adversely affect it. Therefore, if this attitude cannot be changed to at least a neutral position, steroids may not be the contraceptives of choice.