

Ovulation in Non-Lactating Puerpera.

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Menstruation ordinarily reappears in the nonlactating puerperal woman prior to ovulation. Long after the lochia has ceased, anovular bleeding appears, but usually is followed within a few weeks by ovular menstruation. Griffith and McBride,¹ on the basis of endometrial biopsy studies, reported that ovulation was delayed until 5 months or later postpartum in a group of 11 nonlactating patients. These same women showed anovular menstruation at an average of 2 months postpartum.

The present study was undertaken in order to determine the time of reappearance of ovulation in the nonlactating puerpera by means of the basal body temperature technic.² This method of evaluation agrees with direct evidence of ovulation observed at laparotomy.³ Twenty-three nonlactating puerpera charted their basal temperatures until ovulation and menstruation recurred regularly. Endometrial biopsies were taken during the phase of temperature elevation in 7 of the group, and all of these showed progesterational or secretory changes. Menstruation occurred within 2 weeks of the time of biopsy in each case.

As shown in Table I the average time of 8.4 weeks (range 5-15 weeks) for the reappearance of menstruation, agrees with Griffith and McBride's figure of 8 weeks. A significant difference will be noted, however, in the estimated average time of ovulation, which is less accurately determinable. Although the initial menstruation is almost al-

ways anovular, a few patients in this series ovulated prior to menstruation, and their data were, obviously, partially responsible for the low figure of 10.2 weeks (range 6-17 weeks) as contrasted with 20 weeks reported by Griffith and McBride for ovulation.

During the course of these studies, it was observed that when lactation was not carried on, or when it was discontinued very early, anovular bleeding was usually seen prior to the return of ovulation. However, after about the eighth postpartum week ovulation occurred with increasing frequency prior to menstruation. These observations will presumably find explanation in the availability of distinct proportions of pituitary gonadotrophins, adequate in some cases to stimulate the normal cyclic growth sequence in the ovary, culminating in ovulation, and deficient in other instances in which the follicular apparatus does not for a time mature and ovulate, but does form enough hormone to bring about cyclic uterine changes. The appearance of ovulation in these instances seems to imitate the succession of events found at the menarche in that the cycles progressively improve until they resemble the normal pattern. Ovulation probably requires more gonadotrophin than menstruation, and the variation in the amount available in different puerpera during the early weeks of the puerperium is relatively large.

Summary. From the study of basal temperatures, correlated with endometrial biopsy

TABLE I.
Reappearance of Ovulation and Menstruation in the Nonlactating Puerpera.

No. of cases	Onset menstruation in avg weeks post-partum	Onset ovulation in avg weeks post-partum
23 (this report)	8.4	10.2
11 (Griffith and McBride)	8.0	20.0

¹ Griffith, L. S., and McBride, W. P. L., *J. Mich. M. Soc.*, 1939, **38**, 1064.

² Rubenstein, B. B., *Endocrinology*, 1938, **22**, 41.

³ Greulich, W., Morris, E. S., and Black, M. E., *Proc. Conf. Prob. Human Fertility*, 1943, p. 37.

control, the average time for the initial ovulation in 23 nonlactating puerpera was found to be 10.2 weeks postpartum. There is considerable variation in the appearance time of ovulation in the absence of lactation. This

may be attributed to varying degrees of gonadotrophic stimulation, sufficient in some cases to culminate in ovulation as early as the sixth postpartum week.

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Growth Retardation and Corneal Vascularization with Tyrosine and Phenylalanine in a Purified Diet.

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In a previous study dealing with the antagonistic action of certain amino acids toward the growth of *Streptococcus bovis* in a synthetic medium, it was found that a combination of *dl*-phenylalanine and *l*(-)-tyrosine showed a marked inhibitory effect.¹ This inhibition of growth could be counteracted by the addition of *l*(-)-tryptophane to the medium. Increased amounts of nicotinic acid added to the medium showed no effect. Krehl, Teply, Sarma, and Elvehjem² have shown that growth retardation in rats produced by the addition of corn grits to the diet could be counteracted by adding a small amount of tryptophane or nicotinic acid to the diet. In view of this fact the work with amino acid antagonisms was extended in order to determine whether the same phenomenon could be demonstrated in rats.

The following basal ration, similar to that used by Krehl *et al.*² was used: Labco vitamin-free casein 10, sucrose 83, corn oil 3, U.S.P. salt I 4, and cystine 0.15 parts. Vitamins were incorporated in the basal ration in the following amounts: thiamine 0.2, riboflavine 0.3, pyridoxine 0.25, calcium pantothenate 2.0, choline chloride 100, inositol 10, 2-methylnaphthaquinone 0.1, biotin 0.01, and folic acid 0.0115 mg per 100 g. Halibut

liver oil (diluted 1:2 with corn oil) was fed at a level of 2 drops per week, with α -tocopherol included at 0.5 mg per drop. Additions to this diet were made by replacing an equal weight of sucrose. Substances added to the basal diet were thoroughly mixed with it using a mortar and pestle. Weanling, male rats averaging from 45 to 55 g were used throughout these experiments. Five rats were placed on each diet except in the case of a few control diets in which 3 were used.

The addition of 1% *dl*-phenylalanine and 1% *l*(-)-tyrosine to the basal ration produced a substantial growth retardation (Table I) which was accompanied in about 50% of the cases by vascularization of the cornea and marked edematous swelling of the feet. With the addition of levels of phenylalanine and tyrosine as high as 2% each, growth was almost completely inhibited over a 3-week period. At this higher level more severe external lesions were noted and they occurred in 100% of the cases. Spontaneous healing of the external lesions was noted with all of the levels used in these experiments. When 2% phenylalanine and 2% tyrosine were used, the lesions began to appear on the 6th day and healing became apparent on the 15th to 18th day.

Contrary to the results obtained with *Streptococcus bovis*, it was found that the addition of tyrosine or phenylalanine alone to the basal ration produced growth retardation and external lesions to an extent which

¹ Niven, C. F., Jr., and Washburn, Mary R., unpublished.

² Krehl, W. A., Teply, L. J., Sarma, P. S., and Elvehjem, C. A., *Science*, 1945, **101**, 489.