# Plasma Lipid Levels During Pregnancy in the Rhesus Monkey (*Macaca mulatta*) (35957)

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Blood lipids have been studied during pregnancy in a number of mammalian species (1–4). In the dog, rat, and human a hyperlipemia occurs, while the pregnant baboon is hypolipemic. Although certain of the blood constituents in both normal (5, 6) and pregnant (7) rhesus monkeys have been studied extensively, little is known regarding blood lipid moieties. Wolf *et al.* (8) clearly demonstrated a marked depression in plasma cholesterol in the pregnant rhesus monkey. In view of this lack of information, it appeared desirable to quantify the principal blood lipids and to establish more clearly the changes that occur during pregnancy in the rhesus monkey.

*Materials and Methods.* Eight cycling female rhesus monkeys of varying parity were used in this study. Blood samples were obtained at weekly intervals from all animals beginning 5 weeks prior to mating and ending 3 weeks after parturition. From five of the animals, a blood sample was obtained within 12 hr after delivery; fourth week postpartum samples were also taken from these animals. Blood collections were made approximately 15 hr postabsorptively. All samples were centrifuged within 30 min after removal and the plasma was analyzed either the same day or frozen and stored at −17° until processed.

All monkeys were fed a standard laboratory diet as previously described (9). The conception date of all animals was known and the average gestation period was 167 ± 2 (SEM) days. Newborn infants were removed from their mothers within 12 hr after birth. Total lipids were analyzed by the method of Bragdon (10), triglycerides as outlined by Lofland (11), fatty acids as described by Antonis (12), and total cholesterol according to Bowman and Wolf (13). Phospholipids were determined as lipid phosphorus by a modification of the method of Chen *et al.* (14) using 30% $H_2O_2$ (0.0005% phosphorus contamination) instead of 70% $HClO_4$ in the digestion phase.

*Results. Cholesterol.* The nonpregnant level of plasma total cholesterol was 145.4 ± 4.8 mg/100 ml (Fig. 1). This level remained relatively constant for the first 5 weeks of pregnancy, and then decreased significantly ($p<.001$) to 82.6 ± 5.1 mg/100 ml by week 9. The maximum depression occurred during week 16, the 72.9 ± 6.0 mg/100 ml value observed being about half that seen in the nonpregnant monkey. Within 12 hr following parturition, plasma cholesterol concentration increased to 101.3 ± 9.5 mg/100 ml, but was still significantly lower than nonpregnant values. Within 1 week postpartum, normal nonpregnant concentrations of cholesterol were observed.

*Phospholipids.* The plasma concentration of phospholipids in nonpregnant monkeys was 213.4 ± 5.1 mg/100 ml (Fig. 1). Alterations in this lipid moiety were initially observed after the fifth week and were significantly decreased ($p<.001$) to 158.4 ± 12.4 mg/100 ml by the ninth week. A maximum depression to 119.4 ± 9.4 mg/100 ml during week 12 represented a decline to essentially half the concentration observed in the nonpregnant animal. Beginning with week 17, plasma phospholipids increased slightly, but were still significantly lower ($p<.01$) than control values. Within 12 hr after parturition, however, a steep rise in phospholipids

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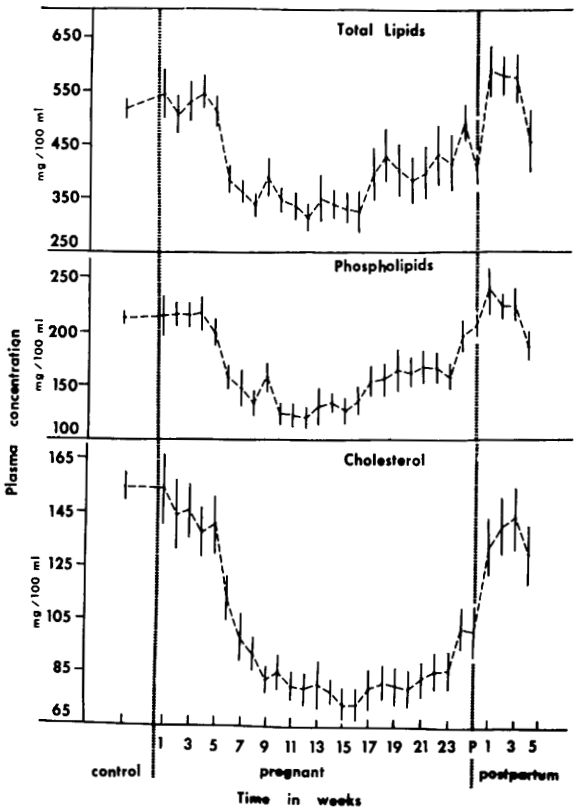


FIG. 1. Weekly fluctuations in plasma total lipid, phospholipid, and cholesterol levels during pregnancy and postpartum in the rhesus monkey. Data in Figs. 1 and 2 are based on means ± SE of eight monkeys, except for the parturition and 4-week postpartum samples, where $n = 5$.

was observed; the mean of 205.6 ± 9.6 mg/100 ml was not different from nonpregnant levels. These values were maintained throughout the third postpartum week.

*Total lipids.* Plasma total lipids prior to pregnancy averaged 517.6 ± 15.3 mg/100 ml (Fig. 1). During pregnancy, there was a sharp decline starting at week 6, decreasing significantly ($p<.01$) to 390.2 ± 34.1 mg/100 ml during week 9. A low of 311.9 ± 27.0 mg/100 ml was reached at week 12 ($p<.001$); this was 40% below the nonpregnant level. Little fluctuation was noted during the remainder of pregnancy, and at parturition total lipids were significantly decreased ($p<.02$) from nonpregnant levels. By the first week postpartum, nonpregnant concentrations were again observed.

*Nonesterified fatty acids.* The control level observed prior to mating was 39.3 ± 2.6 μEq/100 ml (Fig. 2). Fluctuation about this value during pregnancy was apparently random until week 17, when the significantly elevated ($p<.01$) value of 58.7 ± 9.2 μEq/100 ml marked the beginning of a gradual elevation in fatty acids which continued through parturition in most of the animals. In spite of the rather large animal variability at this time, the parturition value of 74.0 ± 12.4 μEq/100 ml was almost twice the value that was observed prior to pregnancy ($p<.001$).

*Triglycerides.* Plasma triglycerides also fluctuated randomly during most of pregnancy. The nonpregnant control value was 117.6 ± 5.3 μEq/100 ml, and variations about this value were not significant until week 20 (Fig. 2). From this time onward to the second month postpartum, animal variation was rather large, but mean values were elevated

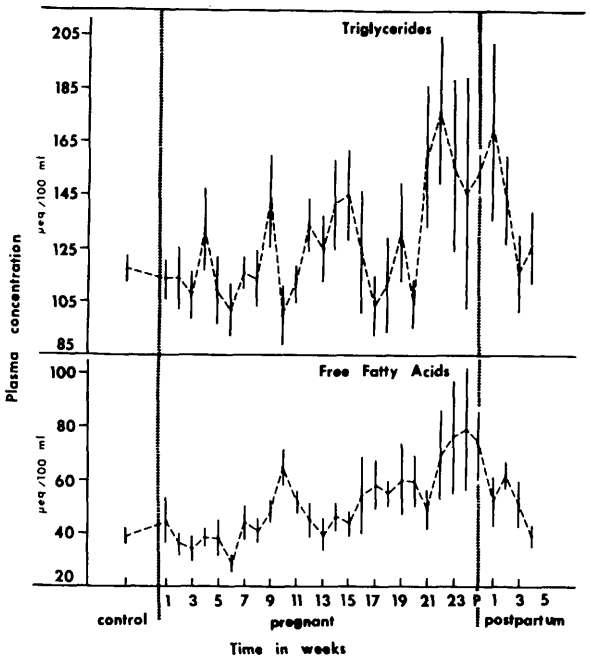


FIG. 2. Weekly fluctuations in plasma triglyceride and free fatty acid levels during pregnancy and postpartum in the rhesus monkey.

above control levels until the second postpartum week, when essentially nonpregnant values were regained.

*Discussion.* The net hypolipemia observed during pregnancy in the rhesus monkey reflects mainly a hypocholesterolemia and hypophospholipidemia. At present, no clear explanation for these results can be offered. It is not possible to account for the decrease in these lipids on the basis of a dilution phenomenon. Although Allen and Ahlgren (7) have demonstrated an increase in plasma volume during pregnancy in the rhesus monkey, this increase only occurs during the second half of gestation and therefore does not account for the marked hypolipemia seen during the initial stages of pregnancy. Since the diet of these animals was constant during pregnancy, the possibility of a varied lipid intake or some nutritional alteration as a result of this may be ruled out as contributory factors.

Since cholesterol is involved in the synthesis of steroid hormones, it is tempting to ascribe the hypolipemia, in part, to an altered requirement for cholesterol in steroid hormone production. Cholesterol and phospholipid levels both begin to decline significantly in the rhesus monkey just as the placenta is changing its role in hormone production from that of protein secretion to primarily steroid production. It has been clearly shown that monkey chorionic gonadotropin levels in the urine cannot be detected after day 39 following mating (15); presumably steroid production by the placenta is beginning at this time. Cholesterol and phospholipid levels are beginning their rapid initial depression by the end of 6 weeks of gestation, just over 40 days following mating. If increasing quantities of cholesterol are required once this changeover has been made, depressed cholesterol levels during this period might be expected. This would appear to be rather different from the situation in the human, where a similar placental changeover to steroid production occurs, followed some time later by a conspicuous elevation of serum cholesterol and phospholipid levels (16).

It is possible that the large triglyceride concentrations seen especially during the later weeks of pregnancy may be due to the

elevated estrogen production which is increased at this time (17). The later stages of human pregnancy are also characterized by a hypertriglyceridemia accompanied by elevated estrogen levels. Women taking oral contraceptives can develop a moderate (18) to severe (19) hypertriglyceridemia and the estrogen component of the pills has been suggested as being responsible for this effect. The mechanism of this effect is at present conjectural.

The liver has long been suspected as playing a role in lipid metabolism during pregnancy insofar as its role in bile production is concerned. Lipids are heavily concentrated in bile, especially cholesterol and phospholipids, and alterations in gallbladder function during pregnancy can lead to sizable fluctuations in plasma lipids. Indeed, in the human there is evidence of a gestational biliary stasis (20); however, this idea has been recently questioned (21). Elevation of excretion rates of lipids via the bile, especially cholesterol and phospholipids, could explain some of the observed alterations, but essentially no data are available in this regard.

*Summary.* A significant decrease in plasma phospholipids, total cholesterol, and total lipids occurs during pregnancy in the rhesus monkey. These alterations are initially observed after week 5 of gestation, reach a maximum by week 11, and are maintained at this level essentially throughout pregnancy, with a small upward trend noted during the terminal few weeks. Nonesterified fatty acid and triglyceride levels fluctuate randomly during most of pregnancy but are elevated during the last month of gestation and at parturition. All lipid moieties return to nonpregnant levels by the second postpartum week.

This investigation was supported by Ford Foundation Grant 63-505 and by National Institutes of Health Grant FR-0167.

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Received June 23, 1971. P.S.E.B.M., 1971, Vol. 138.