

LIPID METABOLISM IN PREGNANCY. II.

(Ratio of Free Cholesterol to Ester Cholesterol and Total Cholesterol to Phospholipids in Normal and Abnormal Pregnancy*)

by

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Introduction

Fat metabolism in the adult male and female has presented some interesting problems and more so in the pregnant female. In general, serum lipids begin to increase during the second trimester and increase progressively as pregnancy advances (Peters *et al*, 1951; Watson, 1957; De Alvarez *et al*, 1959). The rise in lipids during pregnancy is not greatly influenced by diet (Mullick *et al*, 1964; and Green, 1966). Much work has been done on cholesterol and its fractions by various workers and all have found elevated levels in pregnancy (Boyd, 1936; De Alvarez, 1961; Oliver and Boyd, 1955; Smith *et al*, 1959; Burt, 1960; Russ *et al*, 1954). An attempt was made to correlate the cholesterol-phospholipid relation in these conditions as the reports in literature are not consistent (De

Alvarez and Bratvold, 1961; Arsoba and Kretowicz, 1963; and Kontinen *et al*, 1964). Changes in total cholesterol may or may not involve a change in the percentage of free and ester cholesterol: for instance, in certain clinical conditions like diabetes, nephrosis and myxoedema, although the total cholesterol increases, the ratio of free to ester cholesterol does not change, whereas in liver disease, the percentage of ester cholesterol decreases (Verley, 1962). Although in pregnancy the changes in cholesterol and its esters are well known, the percentage change of the free and ester cholesterol or their ratio were not well established. The same is the case with various complications. In the present paper, emphasis is made on these ratios.

Material and Methods

The material and method of collection of blood sample are the same as those described in Part I of this series.

Methods

Total cholesterol was estimated by the ferric chloride and sulphuric acid method of Zlatkis *et al* (1953). Free cholesterol was precipitated with 1% digitonin and estimated as in the case

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of total cholesterol, whereas the esterified cholesterol, ratio of free to esterified cholesterol was deduced from the above values.

Results

Total cholesterol, free cholesterol, esterified cholesterol, ratio of free to ester cholesterol and ratio of total cholesterol to phospholipid contents, in sera of all the three groups of patients are presented in Tables I, II, III, IV and V respectively.

TABLE I
Total Cholesterol in normal and abnormal pregnancy
(mgm. per 100 ml. of serum)

No. of cases	Non-pregnant 25	Normal pregnancy 25	Abnormal pregnancy 25
Range	87.2—285.4	198.2—403.9	181.1—499.9
Mean	154.98	254.83	278.46
S.D.	±59.18	±48.75	±63.99
't'*	—	6.38+	7.01+
't'l**	—	—	1.45

+ Significant.

*t compared to non-pregnant group.

**t1 compared to normal pregnancy group.

TABLE II
Free Cholesterol in normal and abnormal pregnancy
(mgm. per 100 ml. of serum)

No. of cases	Non-pregnant 25	Normal pregnancy 25	Abnormal pregnancy 25
Range	19.50—58.20	37.9—111.0	59.6—138.0
Mean	36.05	89.88	92.37
S.D.	±13.25	±17.15	±25.02
't'*	—	12.25+	9.77+
t'l	—	—	0.44

+ Significant

*t compared to non-pregnant group.

**t1 compared to normal pregnancy group.

TABLE III
Esterified Cholesterol in normal and abnormal pregnancy
(mgm. per 100 cc. of serum)

No. of cases	Non-pregnant 25	Normal pregnancy 25	Abnormal pregnancy 25
Range	45.75—243.6	115.6—298.9	110.5—322.0
Mean	119.30	164.92	179.14
S.D.	±57.81	±43.53	±57.62
't'*	—	3.12+	3.63+
't'l**	—	—	0.97

+ Significant.

*t compared to non-pregnant group.

**t1 compared to normal pregnancy group.

TABLE IV
Ratio of Free Cholesterol to Ester Cholesterol in normal and abnormal pregnancy

No. of cases.	Non-pregnant 25	Normal pregnancy 25	Abnormal pregnancy 25
Range	0.10—0.82	0.22—0.80	0.32—0.92
Mean	0.35	0.55	0.59
S.D.	±0.18	±0.18	±0.22
't'*	—	3.57+	3.70+
't1' **	—	—	0.70

+ Significant.

*t compared to non-pregnant group.

**t1 compared to normal pregnancy group.

TABLE V
Ratio of Total Cholesterol to Phospholipid in normal and abnormal pregnancy

No. of cases.	Non-pregnant 25	Normal pregnancy 25	Abnormal pregnancy 25
Range	0.30—1.20	0.65—1.80	0.44—1.70
Mean	0.82	0.93	0.94
S.D.	±0.26	±0.41	±0.29
't'*	—	3.66+	5.29+
't1' **	—	—	0.99

+ Significant.

*t compared to non-pregnant group.

**t1 compared to normal pregnancy group.

The levels of total cholesterol and its two fractions, free and ester, were significantly higher in normal as well as in pathological pregnancy than in those of the non-pregnant group. The mean value for the ratios of free to ester cholesterol (Table IV) also was increased in the normal and toxæmic pregnant women as compared to the non-pregnant controls. The same is the case with the ratios of cholesterol to phospholipids (Table V). A uniform increase in all fractions of cholesterol in the toxæmic group from those of normal pregnant group was observed, as in the case of total lipids and phospholipids in the previous paper (Part I of this series). However, neither the ratios of free to ester cholesterol nor that of cholesterol to phospholipid did show any sig-

nificant change in these patients from those of the normal pregnant group. The two cases of diabetes and one case of nephrotic syndrome showed very high total cholesterol (301.6, 295.2 and 449.4 mgm per 100 ml. respectively). The free and ester cholesterol in these diabetic cases were 65.49, 65.49, 236.11 and 229.7 mgm% respectively, and in nephrotic case the respective values were 127.4 and 322.0 mgm%. The ratio of free to ester cholesterol in the former was 0.23 and 0.28 and TC/PL ratio was 0.34 and 0.53 respectively. In the nephrotic pregnant woman these ratios were 0.39 and 1.7 respectively.

Discussion

The present observations indicate a uniform rise in cholesterol, both

free and esterified fractions, in normal and toxæmic pregnancies, from those of normal non-pregnant controls. Although the increase in total cholesterol in normal and toxæmic pregnancy is inconsistent with the previous studies (references cited in introduction), the ratio of free to esterified cholesterol increased, like cholesterol to phospholipid ratio in the present investigations. Quinto *et al* (1967), and previous workers (Tyler and Underhill, 1925; Gardner and Gainsborough, 1929; Boyd, 1934; Schwarz *et al*, 1940) reported that during pregnancy the free to esterified cholesterol ratio does not change, whereas the phospholipid to cholesterol ratio rises progressively to reach almost unity in the last trimester.

However, Arsoha and Kretowicz (1963) and Konttinen *et al* (1964) found no change in TC/PL ratio in toxæmia of pregnancy, although both cholesterol and phospholipids were elevated. An increase in FC/EC ratio in normal pregnancy suggested that esterification of cholesterol is markedly decreased or the hydrolysis of the cholesterol esters is increased. An increase in lipolytic activity could be attributed partly to the reduced capacity of the tissues to metabolize glucose as evidenced by a remarkable rise in serum ketone bodies during uncomplicated pregnancy (Quinto *et al*, 1967). Nevertheless, the changes in the toxæmic women were similar to the normal pregnant women in this respect (Tables IV and V). In the case of diabetic pregnancy findings are interesting in the respect that the FC/EC and TC/PL ratios are decreased significantly from the normal preg-

nant ones, showing a great increase in phospholipids, and esterified cholesterol.

These findings are contradictory to those of non-pregnant diabetic patients where the ratios are not changed (Varley, 1962).

Summary

(1) The serum cholesterol, total and free, and the ratio of free to esterified cholesterol and total cholesterol to phospholipid have been studied in 25 subjects each of non-pregnant, pregnant and toxæmic women, 2 diabetic pregnant women and 1 nephrotic pregnant woman.

(2) The total cholesterol and the ratios of FC/EC and TC/PL were significantly increased both in normal and toxæmic pregnancy as compared to the non-pregnant women. On the contrary the diabetic patients showed a decrease in these ratios although the total cholesterol was elevated markedly from those of non-pregnant and pregnant women.

Conclusion

The present study revealed, that although an increase in total cholesterol resulted from an elevation of both free and ester fractions in normal pregnancy and in various pathological states, the cholesterol metabolism seemed to differ in each condition. It seemed to be similar in normal and toxæmic pregnancy, showing high FC/EC and TC/PL ratios, whereas the diabetic pregnant women showed a decrease in these ratios. The differences in the metabolism of cholesterol in the diabetic pregnant women from those of normal pregnant, diabetic non-pregnant or dia-

betic men warrant further elucidation.

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