

LIVER FUNCTION TESTS IN WOMEN USING ORAL CONTRACEPTIVE

by

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and

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The utility of the oral contraceptive is well established in the control of birth rate. Large number of workers have studied their side effects (Elton and Nutting, 1961; Pincus, 1962; Holmstrom, 1965; Andrews and Andrews, 1964, 1965). Several workers have also studied the effects of oral contraceptive on the liver function tests (Schaffner *et al*, 1959; Eisalo *et al*, 1964; Palva and Mustala, 1964; Sotaniemi *et al*, 1964; Rice-Wray *et al*, 1962; Swaab, 1964; Swyer and Little, 1964; Borglin, 1965; Culberg *et al*, 1965; Stoll *et al*, 1966). But the results of these authors were based on the study conducted in women who were taking oral contraceptive for a short duration and the results are controvertial. The present study of the important liver function tests have been taken up in women who had been taking the oral contraceptive for the last three years or less.

Material and Methods

The women, of varying ages included in the present study, were attending the Family Planning Centre of the J.L.N. Medical College Hospital, Ajmer. The

pill taken was Ovulen and each tablet contained 1 mg. ethynodiol diacetate and 0.1 mg. mestranol manufactured by M/s. G. D. Searle & Co., U.S.A. The women were divided into 4 groups as follows:

Group I: 29 Women to act as controls.

Group II: 22 Women using oral contraceptive for the last one year.

Group III: 22 Women using the pill for the last 2 years.

Group IV: 14 Women using the oral contraceptive for the last 3 years.

Each woman had complete physical examination, including haemoglobin, total RBC and total WBC estimations. To assess the liver function, total serum protein, A.G. ratio, bilirubin, icteric index, thymol turbidity, and total cholesterol estimations were carried out.

Venous blood was obtained from each patient by a standard technique. Total protein and A.G. ratio were determined by Biuret method (Wootton, 1964), bilirubin was estimated by Vanden Berg Method (King 1950) and thymol turbidity was estimated by the method of Maclagan, 1944. Icteric index was estimated by colorimetric method Gradwchl's method, 1963. Cholesterol was determined by the method of Bloor, Pelkan and Allen, 1922.

Results are given in Table I.

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TABLE I
 Showing the Liver Function Tests in Normal Subjects and Subjects using
 Oral Contraceptives in Groups II, III and IV

| S. No. | Subjects No. of cases | Total protein G/100 ml. | A.G. Ratio | Bilirubin mg/100 ml. | Icteric index units | Thymol turbidity units | Cholesterol mg/100 ml. | |
|--------|--------------------------|----------------------------|---|--|---|---|--|--|
| 1. | Control Group I | 29 | 6.2 ± .04 (5.2-7.00) | 1.49 ± .03 (1.2-1.8) | 0.42 ± .025 (.30-.64) | 4.7 ± 0.19 (2.0-8.0) | 1.1 ± .057 (1.00-2.0) | 162.0 ± 5.42 (115.4-227.2) |
| 2. | Group II | 22 | 6.8 ± 0.10 (6.0-7.6) t = 3.7 P < .05 | 1.5 ± .04 (1.1-1.8) t = 0.5 P > .05 | 0.52 ± .06 (.2-1.6) t = 0.9 P > .05 | 5.0 ± 0.32 (2-8) t = 1.0 P > .05 | 4.3 ± 0.39 (2-7) t = 10.6 P < .01 | 254.4 ± 8.4 (190-340) t = 54.3 P < .001 |
| 3. | Group III | 22 | 6.8 ± 0.11 (5.4-7.5) t = 3.7 P < .05 | 1.42 ± .04 (1.0-1.7) t = .16 P > .05 | 0.45 ± .003 (.3-1.0) t = .42 P > .01 | 5.1 ± 0.32 (3-7) t = 1.4 P > .05 | 3.8 ± 0.32 (2-8) t = 10.3 P < .01 | 239.1 ± 6.8 (190-300.0) t = 48.1 P < .001 |
| 4. | Group IV | 14 | 6.4 ± 0.24 (5.0-7.3) t = 0.7 P > .05 | 1.45 ± .07 (1.0-1.9) t = 0.25 P > .05 | 0.46 ± .05 (.3-1.0) t = 0.36 P > .05 | 5.2 ± .23 (3-6) t = 1.7 P > .05 | 3.6 ± .43 (2-8) t = 7.8 P < .01 | 231.4 ± 6.6 (190-330) t = 39.4 P < .001 |

Values are mean, ± S.E., Figures in parenthesis show range.

Discussion

In the normal subjects (Group I) the total protein ranged from 5.7 to 7.0 G/100 ml. with a mean value of 6.2 G/100 ml. In Group II the serum total protein level ranged from 6.0 to 7.6 with a mean value of 6.8 G/100 ml., in Group III the serum protein ranged from 6.0—7.6 with a mean value of $6.8 \pm$ and in Group IV the serum protein level ranged from 5.0—7.3 with mean value of 6.4. Thus, in the subjects using oral contraceptive for one to two years, the serum protein concentration was increased by 9.6% which is significant statistically ($P < .05$). However, in the Group IV cases, the serum protein level was found to be increased but it was not significant statistically.

The initial increase in the serum protein level thus can be accounted for, either as an anabolic effect of steroid hormone, or parenchymal liver damage which may elicit a rise in globulin, thereby increasing the total protein content.

However, the A. G. Ratio determination showed no significant change in the A. G. Ratio, in all the 3 groups as compared to Group I. Similar findings have also been reported by Orellane, *et al* (1966) and Bakke (1965). This suggests that there is no rise in globulin fraction of total serum protein, thus ruling out the possibility of any parenchymal liver damage and the only other possible hypothesis is anabolic action of the oral contraceptives.

The serum bilirubin in the control group ranged from 0.30-0.64 mg/100 ml. with a mean value of 0.42 mg/100 ml. while in the subjects of Group II, III and IV the serum bilirubin ranged from 0.2-1.6 (mean 0.52), 0.3-1.0 (mean 0.45) and 0.3 to 1.0 (mean 0.46) respectively. Thus, there is a slight rise in all the three

groups in the bilirubin values. However, the rise is not significant statistically. The same findings have been reported by Bakke (1965), Swyer and Little (1965), Swaab (1964), Linthorst (1964), Ockner and Davidson (1967), Stoll (1966) and Eisalo *et al* (1965). The slight rise in serum bilirubin level might be due to adjustment of the liver function to the altered hormonal milieu. It reflects no liver damage, which is further supported by icteric index determination (Table 1). There is a slight rise within normal limits in icteric index of the subjects of all the three groups using oral contraceptives and was not statistically significant even at 5% probability.

The thymol turbidity values in control subjects ranged from 1-2 units with a mean value of 1.1 units and in the subjects of Group II, III and IV it ranged from 2-7 (Mean 4.3), 2-8 (mean 3.8) and 2-8 (mean 3.6) respectively. It is evident, therefore, that there is rise in the values of thymol turbidity test ($P < 0.01$) in the subjects using oral contraceptive which is highly significant. Linthorst (1964), Fawcett and Pederson (1964), Eisalo *et al* (1965), Larsson-Cohn (1967), Pincus *et al* (1959), Bakke (1965) and Thulin (1966), have also made similar observations and the rise was not more than 4 units. The thymol turbidity test indicates the alteration in the plasma protein fractions, i.e. β - γ globulin which might be due to the action of steroid hormones. Actual changes in the protein fractions are under study by electrophoretic determination and will be reported later on.

In the present study the total cholesterol content of the control group ranged from 115.4-227.7 mg/100 ml. with a mean value of 162.0 and in subjects of the groups II, III and IV the results were

from 190-340 mg/100 ml. with a mean value of 254.4, 190-300 mg/100 ml. with a mean value of 239.1 and 190-330 mg/100 ml. with a mean value of 231.4, respectively. The results show a rise in total cholesterol in the subjects using oral contraceptives which is highly significant ($P < .001$). However, there is a decline in the subjects of Groups III and IV. Schaffner (1966) has reported similar results. The rise may be either due to the increased steroid moiety for the cholesterol synthesis by the oral contraceptives or due to the effect of steroid hormones in releasing more cholesterol from the liver into the blood.

Summary

1. Effect of oral contraceptive on some of the liver function tests in the subjects taking oral contraceptive upto three years duration have been studied.

2. There is a significant rise in the total protein in subjects using the pill upto 2 years duration. The rise is not significant in subjects using oral contraceptives for three years. No statistically significant changes have been found in A.G. Ratio, bilirubin and icteric index.

3. There is significant increase in the thymol turbidity values in all the subjects using oral contraceptives.

4. There is highly significant rise in cholesterol values in all the subjects using oral contraceptives.

Acknowledgements

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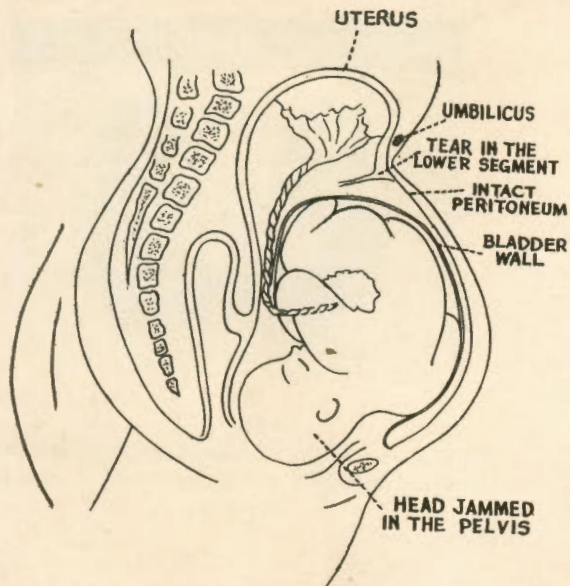


Fig. 1

Baby in bladder after incomplete rupture of uterus.

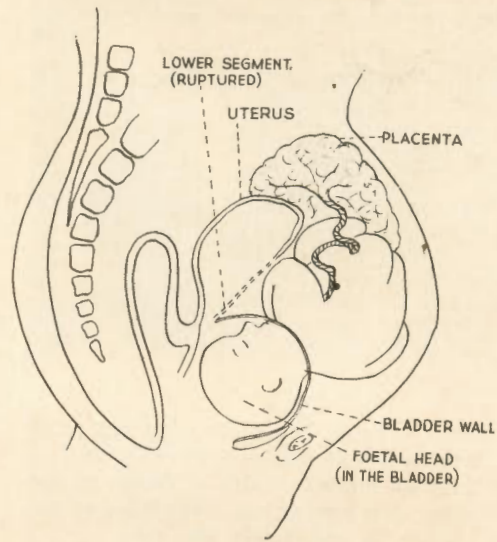


Fig. 2

Foetal head in bladder after complete rupture of uterus.

Prolapse of an Incarcerated—Sasoon and Thankam pp. 570-571

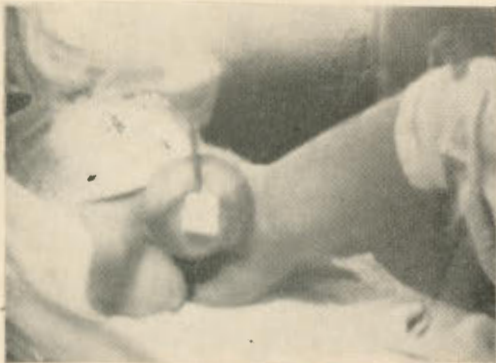


Fig. 1

16 weeks size pregnant uterus prolapsed outside through the pouch of Douglas.

Viable Pregnancy in Unicornuate Uterus—Sen pp. 572-574

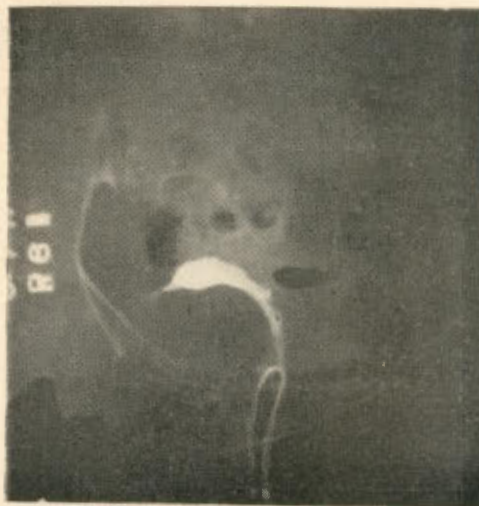


Fig. 1

Hystero salpingogram shows extreme distension of the cornue with spilling through the patent right tube.

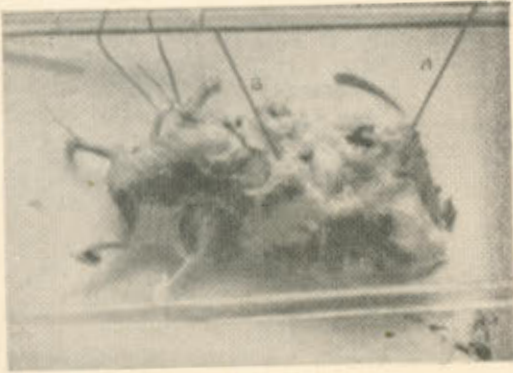


Fig. 1

Photograph of case No. 1 showing distended right tube at its ampullary part with sign of acute rupture through which a foetus of (14 weeks size) seen coming out. The head of the foetus is still inside the tube.

A. isthmial end.

B. abdominal ostium.



Fig. 2

Photograph of the intrauterine twin fetuses. Abortion occurred at 22 weeks of pregnancy (Case I).

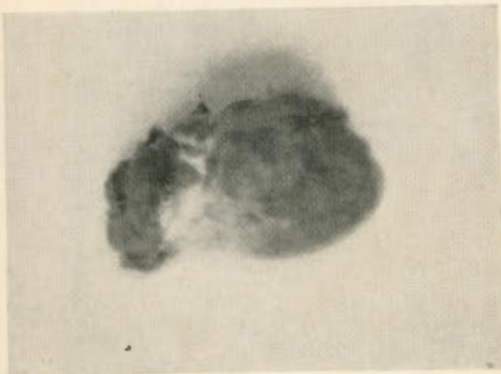


Fig. 3

Incomplete tubal abortion of case No. 2, showing products of conception with blood clots coming out through the abdominal ostium.

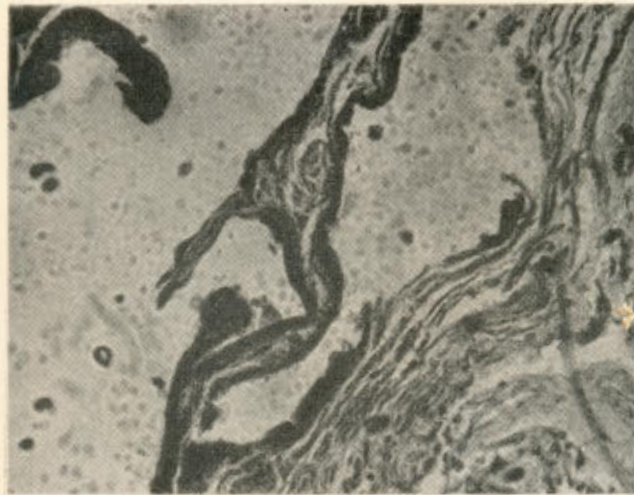


Fig. 4

Section of the tube of case 2 showing adhesions of the plicae and focal collection of round cells suggestive of chronic salpingitis.

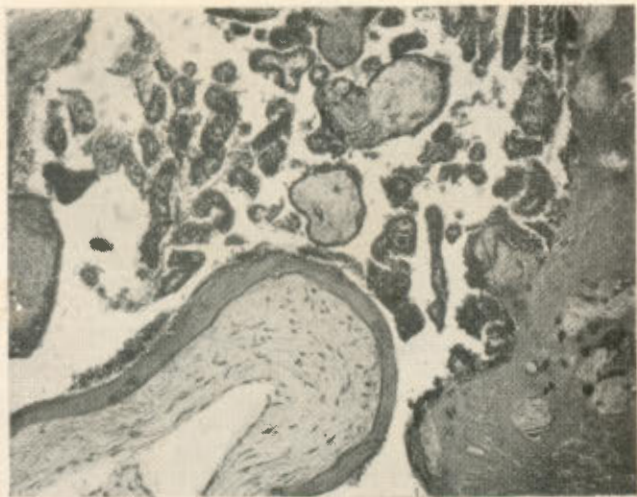


Fig. 5
Section of the fleshy mass passed per vaginam from case No. 2 shows decidual reaction of endometrium with scattered chronic villi suggesting intrauterine pregnancy.

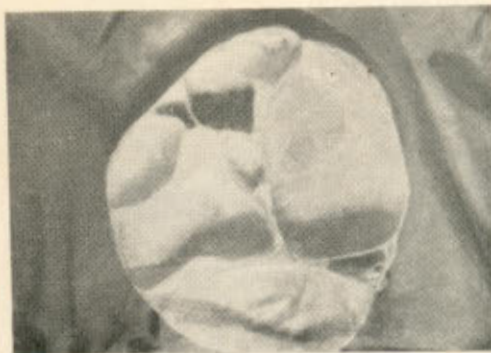


Fig. 1
Showing cut surface of the cystic granulosa cell tumor.

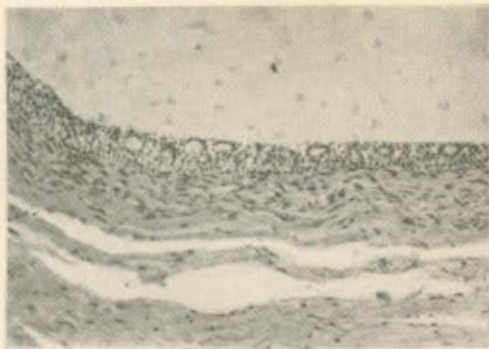


Fig. 2
Showing granulosa cell, call-exner bodies and theca cells in the lining of the cystic granulosa cell tumour (H & E 300).

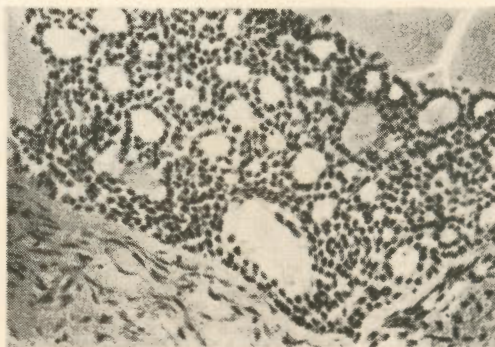


Fig. 3
Showing higher magnification of Fig. No. 2.
(H & E 300).

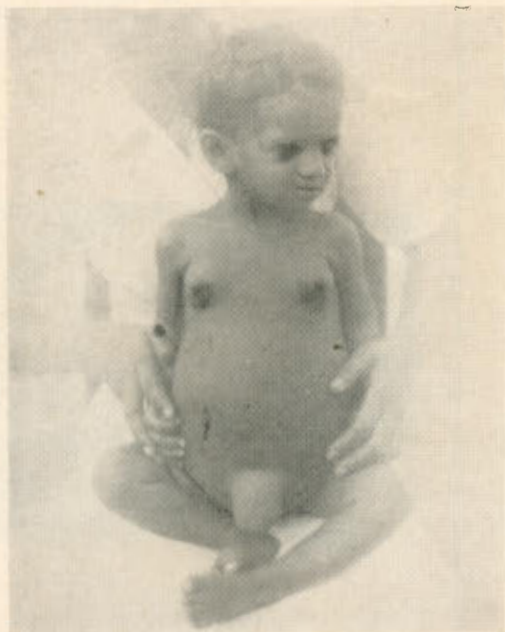


Fig. 1

Girl aged 10 months showing bilateral enlargement of breasts and abdominal distension with a big umbilical hernia.



Fig. 2

Photograph showing well developed external genitalia.

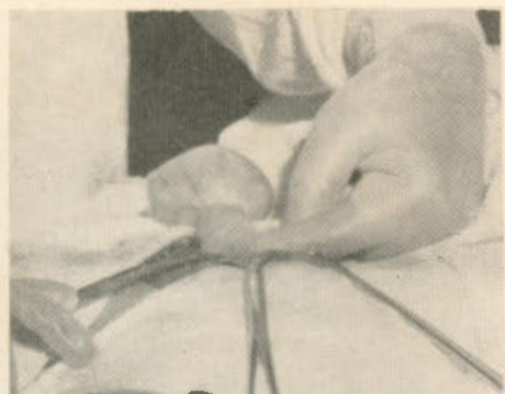


Fig. 3

At operation uterus enlarged in size, right side ovary replaced by a big oval shaped tumor yellowish white in colour.

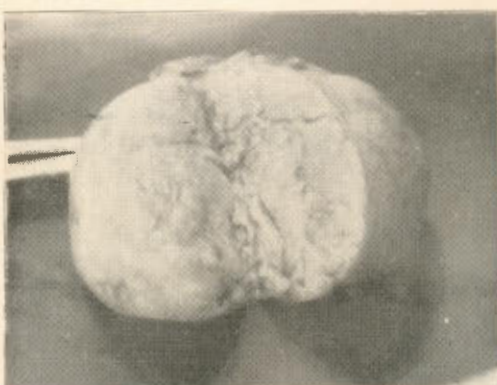


Fig. 4

Macroscopic appearance of cut section of RT ovarian tumor. Sliced tumor mass, yellowish white, well encapsulated.



Fig. 1
Illustrating single amniotic sac with almost joint origin of the two cords.



Fig. 2
Illustrating one normal macerated still born foetus and other foetus with congenital malformation.

Primary Carcinoma of the Fallopian Tube—Chowdhury pp. 586-589

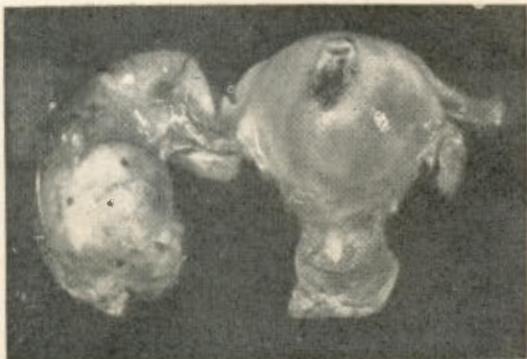


Fig. 1
Uterus with fallopian tubes and ovaries. Right fallopian tube distended with a firm mass arising from the lateral two-third of the tube.

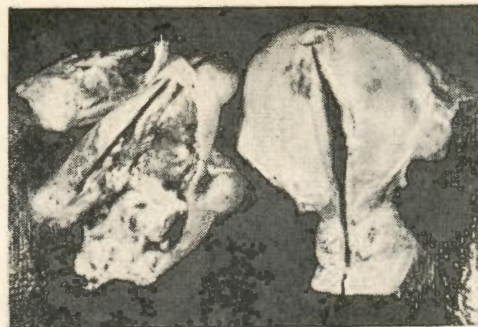


Fig. 2
Uterus cut open showed adenomyosis. Right fallopian tube opened to show a huge fungating and necrotic growth of papillomatous character.