

# STUDY OF ALKALINE PHOSPHATASE ACTIVITY OF HUMAN ENDOMETRIUM IN PATIENTS USING COPPER-T AND LIPPES LOOP AS INTRAUTERINE CONTRACEPTIVE DEVICES

by

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## Introduction

Antifertility effect of metallic copper as an intrauterine contraceptive device have been studied by Zipper (1969) and Chang and Tatum (1970). There is little information about its possible mode of action. One of the widely accepted suggestion about mode of action is that contraceptive effect is due to endometrial changes, resulting in alteration of intrauterine milieu which is rendered hostile to embryo. Hagenfeldt (1972) and Wilson (1972) described a diminution in the endometrial alkaline phosphatase activity during secretory phase of cycle in women using copper-T as IUCD, whereas in women using Lippes loop as IUCD it was observed by Joshi and Sujan (1969) that there was increased activity in secretory phase.

## Methods

The alkaline phosphatase activity was studied in endometrium of patients in various phases of the menstrual cycle. The cases were divided into 2 groups:

Group A: Comprised of 25 cases subjected to Copper-T 200 mm insertion.

Group B: Comprised of 25 cases who were subjected to Lippes loop insertion.

Biopsies were taken before the insertion of Copper-T and Lippes loop during the two phases of the menstrual cycle which served as control. After they were subjected to Copper-T and Lippes loop biopsies were again taken in the two phases on the same day on which control biopsies were taken. The endometrium was divided into two portions, one was immediately frozen and the other fixed for histological study. Alkaline phosphatase activity was estimated by Bessy *et al* (1965) and proteins by Lowery *et al* (1951) method and activity was finally expressed as units per mg protein.

## Results

There was a consistent inhibition of alkaline phosphatase activity in endometrium during secretory phase in cases subjected to Copper-T insertion as shown in Table I, but on the other hand activity of alkaline phosphatase was found increased in the secretory phase in patients who were subjected to Lippes loop as shown in Table II. The results of comparative study between Copper-T and Lippes loop are shown in Table III.

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TABLE I  
Comparison of Alkaline Phosphatase Level in Cases Without IUCD and in Cases With Copper-T as IUCD

Alkaline phosphatase level in units/mg protein

	Proliferative Phase			Secretory Phase		
	Mean	Mean Difference	P Value	Mean	Mean Difference	P Value
Without IUCD	70.24			46.48		
With Copper-T	67.28	2.96	0.01	25.88	20.60	0.001

TABLE II  
Comparison of Alkaline Phosphatase Level in Cases Without IUCD and in Cases With Lippes Loops IUCD

Alkaline phosphatase level in units/mg protein

	Proliferative Phase			Secretory Phase		
	Mean	Mean Difference	P Value	Mean	Mean Difference	P Value
Without IUCD	73.24			50.32		
With Lippes Loop	71.16	0.92	0.1	130.44	80.12	0.001

TABLE III  
Comparison of Alkaline Phosphatase Level in Cases Using Lippes Loop and Copper-T as IUCD

Alkaline phosphatase level in units/mg protein

	Proliferative Phase			Secretory Phase		
	Mean	Mean Difference	P Value	Mean	Mean Difference	P Value
Lippes Loop	74.16			130.44		
Copper-T	67.28	6.88	0.1	25.88	104.56	0.001

### Discussion

Alkaline phosphatase is present in considerable amount in human endometrium and uterine secretions (McKay *et al* (1956). Its role in human reproduction is unknown but it possibly plays a part in transporting nutrients to preimplantation blastocyst. Copper-T 200 mg was inserted in 25 cases after study of alkaline phosphatase activity as control.

The decrease in activity of alkaline phosphatase was observed in secretory phase as shown in Table I and is highly significant at  $P < 0.001$  as shown in Table I. Such a change was also observed by Hagenfeldt (1972), Wilson (1973) and Granasell *et al* (1976). Chang and Tatum (1970) showed in laboratory animals that blastocyst development was normal in presence of copper wire but that implantation did not occur suggesting a local action in uterus. Oster (1972) showed immobilisation of spermatozoa in the cervical mucous containing cupric ions.

Wilson (1973) also found inhibition of alkaline phosphatase activity by cupric ions released from metallic copper which plays a role in the interference of metallic activity of the endometrium.

Tamaya *et al* (1976) also observed interference at the steroid binding site of receptor especially in the progesterone receptor which is more affected by the copper ions than in oestrogen receptor. Hence, from this study, it is concluded that alkaline phosphatase activity of human endometrium plays a part in transporting nutrients to preimplantation blastocyst, whereas interuterine contraceptive devices inhibiting the progesterone receptor decrease the alkaline phosphatase activity of human endometrium and uterine secretions which could seriously affect the process of implantation.

Polidoro and Culner (1974) postulated that contragestational effect of copper IUCD in rabbit involves disappearance of embryos and degeneration of any remaining ova.

Endometrial alkaline phosphatase determination was also done in 25 patients during various phases of menstrual cycle, which served as control. The same patients were subjected to Lippes loop application as interuterine device shown in Table II. Again alkaline phosphatase activity was done in the two phases of menstrual cycle which showed cyclic variations. These findings are in conformity with the findings of Joshi *et al* (1969) and Kar and Kamboj (1969) who found increase in alkaline phosphatase activity in the secretory endometrium while there was no change in the proliferative endometrium. They found that final concentration in the treated endometrium remained significantly higher than that of control tissue. Grandsell *et al* (1976) investigated the effect of plastic IUCD experimentally in rabbit endometrium and found complete disappearance of alkaline phosphatase activity. From our observations it shows that mode of action of Lippes loop preventing the implantation is other than interference with enzymatic activity.

### Summary

The alkaline phosphatase activity was studied in 25 cases during proliferative and secretory phases before and after insertion of Copper-T 200 mm. There was decrease in alkaline phosphatase activity in secretory phase after Copper-T insertion. The difference was highly significant at  $P < 0.001$ . Same enzyme study was done in 25 cases before and after insertion of Lippes Loop in both phases of menstrual cycle. The alkaline phosphatase

activity was found increased in secretory phase and the difference is highly significant at P 0.001.

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