

URIC ACID LEVEL OF UTERINE FLUID AND BLOOD OF WOMEN WITH EXCESSIVE UTERINE BLEEDING

by

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Introduction

A marked elevation in the level of uric acid in the intra uterine fluid of women with an IUCD in situ has recently been reported by Das Gupta *et al*, (1971). This preliminary observation has posed a number of questions of fundamental importance. As no published figures are available for the level of uric acid in the blood and intrauterine fluid during the different phases of the menstrual cycle and in lactation amenorrhoea and amenorrhoea following the menopause, this investigation was undertaken to find the answers to these questions and also to see whether any alteration in uric acid levels occurred in cases with excessive uterine bleeding due either to associated pathological conditions such as, fibromyoma or adenomyosis or in cases with dysfunctional uterine bleeding.

Material and Methods

The clinical material for the study was obtained from Queen Mary's Hospital,

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Lucknow. A total of 164 cases were studied of which 42 had normal regular cycles and served as controls. Eleven women had lactational amenorrhoea and 13 women were postmenopausal.

The remaining 93 cases had excessive uterine bleeding which was dysfunctional in 51, and associated with uterine pathology in 42.

After a careful history, complete clinical examination was carried out in every case. The diagnosis of dysfunctional uterine bleeding was made on the basis of negative findings on bimanual and speculum examinations and confirmed by curettage. In all cases where organic pathology was diagnosed the lesion was confirmed at operation. Of the 51 cases of dysfunctional bleeding, 19 were cases of cyclic bleeding showing a secretory endometrium of which 3 showed benign cystic hyperplasia.

For collection of uterine fluid, the patients were kept in lithotomy position and the cervix was visualised using a Sim's speculum and anterior vaginal retractor. The cervix was swabbed with Savlon lotion and its anterior lip held with a volsellum after which a sterilized loop—insertor was directed into the uterine cavity. The fluid from the uterine cavity was sucked into the insertor by the crea-

tion of negative pressure with the help of the piston of the attached syringe. A mild negative pressure was maintained while pulling out the inserter from the cervix. The aspirated fluid was emptied carefully into a graduated conical—bottom centrifuge tube. The average volume of the fluid per subject was 0.2 ml. From each patient blood (3.0 ml) was drawn from the median cubital vein.

The estimation of uric acid was done according to the method described previously (Das Gupta *et al*, 1971). The contamination of the pooled fluid (2-3 patients) with haemoglobin was found to be 20-25 per cent.

Result

The uric acid level of blood and the uterine fluid of controls and of patients suffering from functional uterine bleeding

of functional uterine bleeding of the anovulatory variety interesting changes in uric acid concentration were recorded in the blood. The blood uric acid level in these cases was found to be significantly higher than the level seen in the proliferative phase in control subjects ($P < 0.1$). In the cases with ovulatory bleeding no deviation from the normal level was recorded in the blood. In the uterine fluid, on the otherhand, the uric acid concentration in both groups of cases registered highly significant increase. In the cases of anovulatory bleeding there was about 400% rise in uric acid concentration above the values in the proliferative phase of control subjects, while in the ovulatory cases the rise was 800% higher than that seen in the secretory phase of controls. This is shown in Table I.

TABLE I

Concentration of Uric Acid in Serum and Uterine Fluid During the Menstrual Cycle in Control and Cases of F.U.B.
Uric Acid Concentration (mg/100 ml)

Subjects	Blood		Uterine fluid	
	Proliferative phase	Secretory phase	Proliferative phase	Secretory phase
Control (42 cases)	2.13 + 0.86	2.24 + 0.71	1.03 + 0.33	0.42 + 0.30
Cases of F.U.B.: 51				
(a) Anovulatory 32	3.14 + 0.10	—	3.85 + 0.25	—
(b) Ovulatory 19	—	2.63 + 0.22	—	3.36 + 0.28

* Mean + S.D. with number of patients in parentheses.

are presented in Table I. In controls although blood uric acid during the proliferative and secretory phases did not differ significantly in the uterine fluid, the uric acid level showed a significant variation in the proliferative and secretory phases of the menstrual cycle, being considerably higher in the proliferative phase than the secretory ($P < .01$). In the cases

The uric acid level of blood and uterine fluid of patients with uterine pathology, lactational amenorrhoea and menopause is presented in Table II. The concentration of uric acid in blood of all these categories of subjects was of the same order and comparable to that of the controls. In the uterine fluid the uric acid level in 35 cases of fibromyoma associated with

TABLE II

Uric Acid Content of Serum and Uterine Fluid the Patients With Uterine Pathology, Lactational Amenorrhoea and Menopause

Subjects:	Uric acid concentration (mg/100 ml)	
	Blood	Uterine fluid
I. With Uterine Pathology:		
(a) fibromyoma	2.74 + 0.94 (35)	3.89 + 1.40 (35)
(b) adenomyosis	2.68 + 0.43 (12)	6.54 + 1.70 (12)
II. Lactational amenorrhoea	2.32 + 0.47 (11)	0.47 + 0.23 (11)
III. Menopause	2.45° + 0.68 (13)	0.35 + 0.24 (13)

* Mean + S.D. with number of patients in parentheses.

excessive bleeding, was of the same order as that seen in case of anovulatory functional bleeding.

In women suffering from adenomyosis who came with menorrhagia, the concentration of uric acid in the uterine fluid was even higher than the values in cases of fibromyoma ($P < .01$); in point of fact, the uterine fluid uric acid values in cases of adenomyosis were the highest of all the groups studied.

The uric acid concentration of the uterine fluid of lactational amenorrhoeic and menopausal women was virtually the same and comparable to that of the normal secretory phase.

Discussion

The demonstration of uric acid in the uterine fluid of women was an interesting addition to the list of biochemical constituents of this fluid reported earlier (Das Gupta *et al*, 1971; Kar *et al*, 1968). The present study shows a cyclic change in uric acid concentration of the fluid control subjects, the value during the proliferative phase being significantly higher than that in the secretory phase. The formation of uric acid as the end product of purine metabolism is well known. On these grounds, a rise in uric acid level of

uterine fluid during the proliferative rather than secretory phase is somewhat intriguing. However, it is also on record that during the proliferative phase there is infiltration of leucocytes, mast cells and macrophages into the uterine lumen where they undergo lysis (Yangamachi and Chang, 1963; Bhagat, 1969; Sagiroglu and Sagiroglu, 1970). This could produce a high uric acid concentration in the fluid. It appears that the increase in uric acid concentration of uterine fluid and perhaps also of blood could be related to blood estrogen titre. This is supported by uniform increase in uric acid concentrations of uterine fluid throughout the cycle in cases showing functional uterine bleeding, since endometria of these patients may be exposed to a persistently high level of estrogen (Lloyd, 1969). It is significant that the blood uric acid titre of these cases also tends to be higher than that of the controls.

In uterine pathology associated with bleeding the uterine fluid level of uric acid is found to be significantly higher than that of normal women, although the blood uric acid level does not show any marked rise above the control value. In adenomyosis cases, the uric acid value of the uterine fluid is practically double the

level of patients showing functional uterine bleeding. In contrast, in lactational amenorrhoeic and post-menopausal subjects, the uric acid level in the fluid is comparable to that of the secretory phase in the controls. Since estrogen titre of blood of these categories is known to be lower than normal (Lloyd, 1969), it is reasonable to expect that their uterine fluid uric acid concentration would also be relatively low, if such concentration is at all estrogen dependent.

Thus, it appears that normally the endometrium is the site of production of uric acid. In patients with uterine pathology (e.g. fibromyoma, adenomyosis) the tumour tissue itself may be an additional local source which is responsible for the markedly high value of uric acid in the uterine fluid of these cases. Similarly, the rise in uric acid level of the uterine fluid in presence of an IUCD (Das Gupta *et al*, 1971) may be due to a persistent local foreign body reaction in the endometrium. On this ground, the bleeding episodes in IUCD cases might indeed be due to raised estrogen levels in the endometrium and should respond to administration of progestogen.

Summary

The uric acid level of uterine fluid and blood of 164 women was investigated. Some of these were normal and served as controls, while others were either cases of dysfunctional bleeding or bleed-

ing associated with uterine pathology. In normal healthy subjects (control), the uterine fluid uric acid value was found to be higher during the proliferative phase than in the secretory phase. The concentration of uric acid in the uterine fluid of patients showing bleeding associated with uterine pathology was consistently higher than that of the control proliferative phase. In lactational amenorrhoea and postmenopausal amenorrhoea the uterine fluid uric acid level was the same as that in the normal secretory phase.

The uric acid value of uterine fluid appears to reflect the status of the endometrium and also perhaps the titre of blood estrogen, but this needs to be confirmed by further work.

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