RADIOIMMUNOASSAY OF FSH AND LH AMONG INFERTILE FEMALES

by

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Infertility is one of the oldest human problems. The magnitude of the problem can be judged from the fact that as many as 10 per cent of the couples suffer from sterility of one or other form and anovulation accounts for an estimated 10-15 per cent of infertility problems in women.

Development of radioimmunoassay technique for hormone estimation in physiological body fluids has overwhelmed all other diagnostic procedures, unveiling a new era in the field of gynaecological investigations. The estimation of serum luteinizing and follicular stimulating hormone levels have been found useful in diagnosis of infertility and its management. Radioimmunoassay is not only simple, but offers advantage of high practicability and exquisite sensitivity.

Detection of presence or absence of ovulation and its timing in the menstrual cycle is the corner stone in evaluating an infertile woman. LH surge in serum could be helpful in predetermination of ovulation and can easily be measured by radioimmunoassay. The present study was carried out with the following aims and objectives:

1. To diagnose anovulatory cycles in sterility cases with the help of serum LH and FSH estimation.
2. To differentiate between primary gonadal and pituitary failure.
3. To evaluate the clinical significance of such informations in the management of these patients.

Material and Methods

The present study was carried out in the Sterility Clinic of the Department of Gynaecology and Obstetrics and the Nuclear Medicine Unit of the Department of Medicine, at S.N. Medical College, Agra. Serum Luteinizing Hormone (LH) and Follicular Stimulating Hormone (FSH) were estimated in 30 female cases of established primary sterility and 10 normal healthy and fertile females (Control Group) in reproductive age, by using radioimmunoassay methods.

The following criteria were used for selection of sterility cases.

*Registrar,
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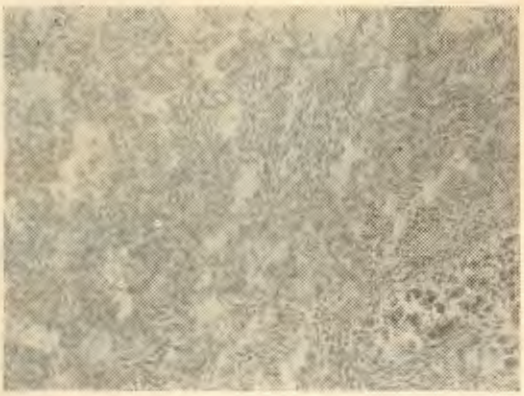

Fig. 1
Histological characteristics of fetal lung of hysterotomy specimen at 20 weeks (control).

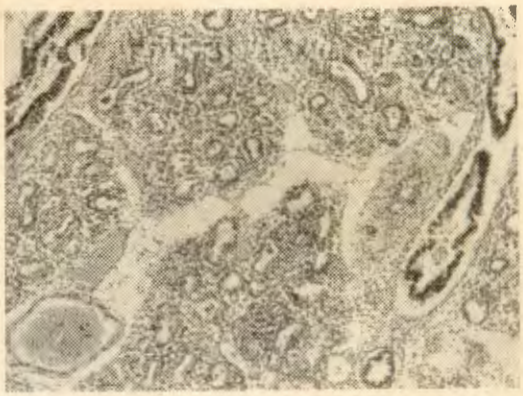

Fig. 2
Histological characteristics of fetal lung following betamethasone instillation at 20 weeks of gestation. Bronchial tree and alveoli are developed.

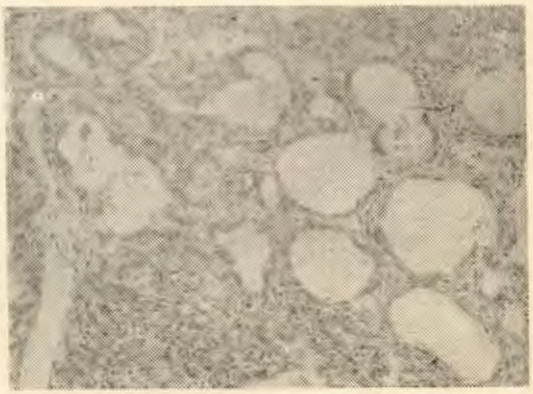

Fig. 3
Histological characteristics of fetal lung following betamethasone instillation at 16 weeks of gestation. Note the aeration of lung tissue.

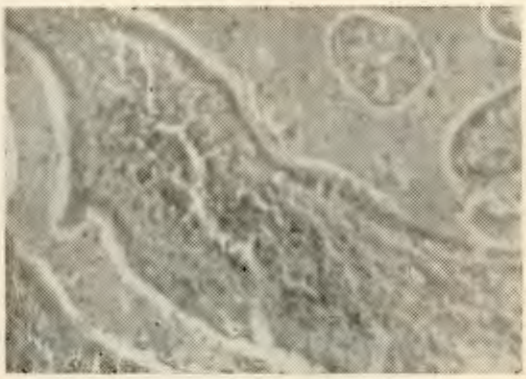

Fig. 1
Showing endometrial glands containing inflammatory exudate in their lumen H & E x 200.

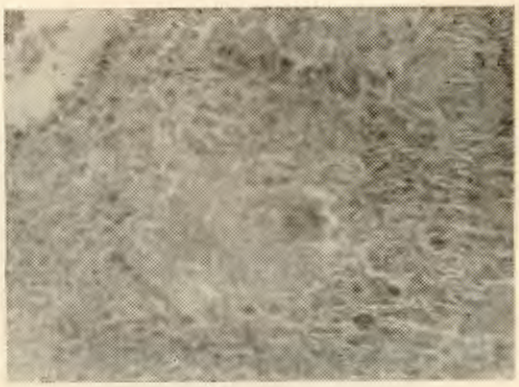

Fig. 2
Granulomatous lesion formed by giant cells & epitheloid cells replacing the glandular epithelium H & E x 200.

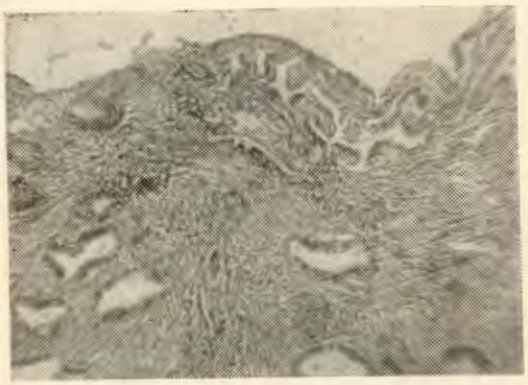

Fig. 3
Showing earliest lesion consisting of lymphatic follicle formation in the stroma near the gland.

Clear Cell Carcinoma of Uterine Cervix—Kalra et al pp. 274-275

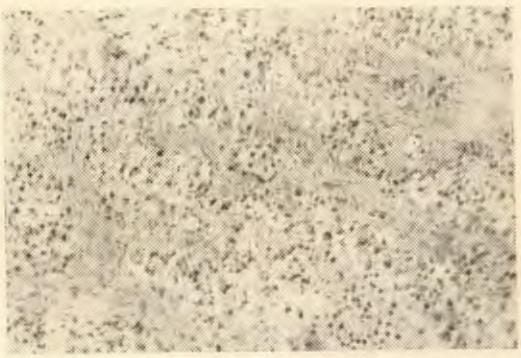

Fig. 1
Low power photomicrograph showing groups of clear cells separated by bands of connective tissue.

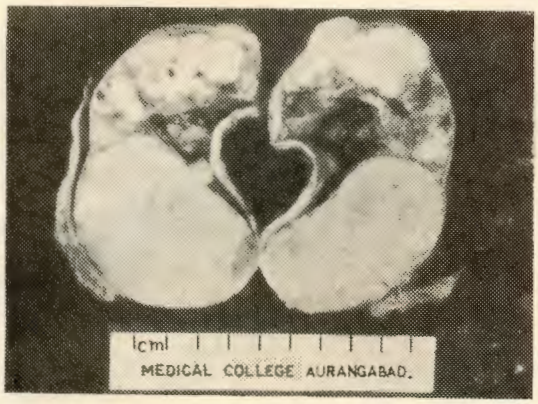

Fig. 1
Photograph showing the cut surface of the dimorphic ovarian tumour. Upper half representing the dysgerminoma and lower oval half, mucinous cystadenoma H & E x 100.

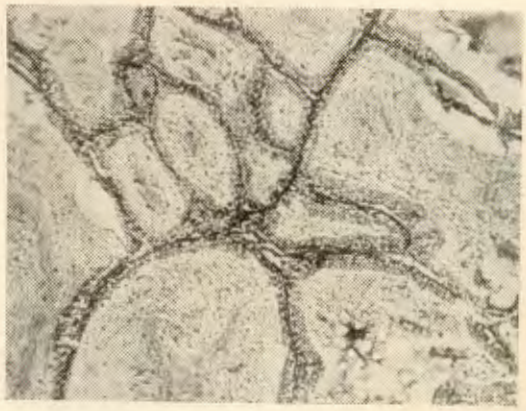

Fig. 2
Photomicrograph showing the mucinous cystaodematous structure, the lining cells being tall columnar with basal nuclei. H & E x 100.

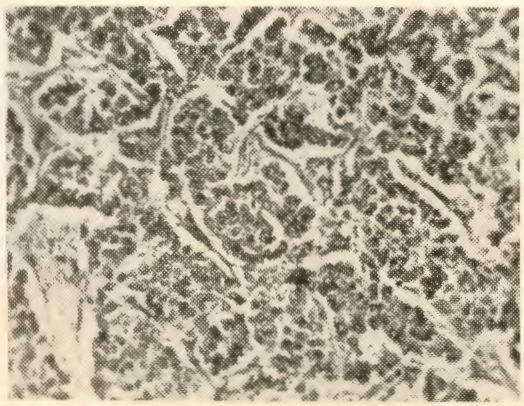

Fig. 3
Photomicrograph showing the structure of dysgerminoma with sheets of cells with large nuclei separated by scanty stroma and having monotonous appearance. H & E x 100.

Torsion of Haematosalpinx with Bicornuate Uterus—Purwar et al pp. 284-285

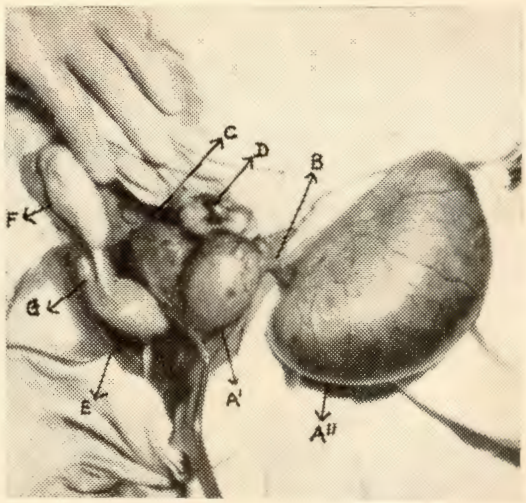

Fig. 1
Shows normal uterus with ovary on left side and right side haematosalpinxs with two twist and other uterus and ovary.

A′= A″ —haematosalpinx
B —twist
C-D —left side uterus & ovary
G —Fallopian tube of right uterus

Rupture Uterus due to Ewings Sarcoma Pubic Bone—S. Garg et al pp. 255-257

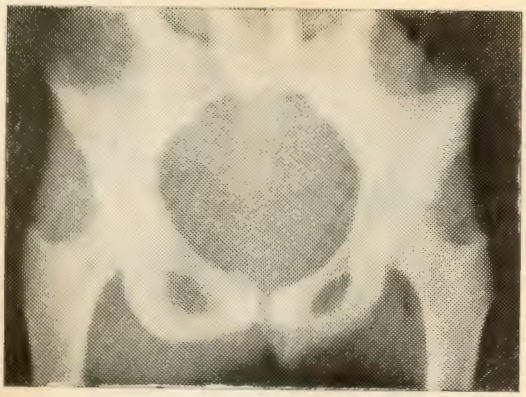

Fig. 1
Shows there is soft tissue swelling around right pubic bone. There is onion peel appearance of peritosteum. Cortex is moth eaten, There is geographical destruction of pubic bone with surrounding sclerosis suggesting Ewings' sarcoma.

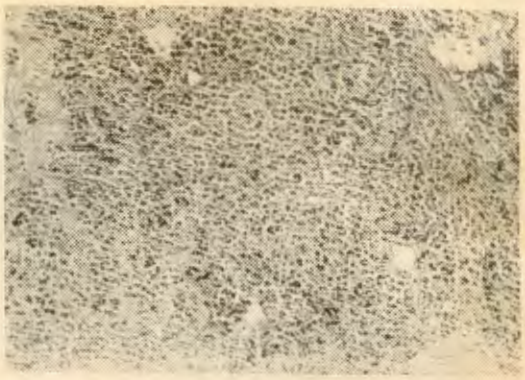

Fig. 2
Shows compact broad sheet of small polyhyderal cells of uniform morphology, with round dark nucleus separated by pale illdefined cystoplasm. The tumour cells show peritheliomatous infiltration around blood vessels of poorly developed fibrovascular stroma. Areas of cell degeneration and necrosis are also present.

Cervical Mucus Response—Raisinghaney et al pp. 228-231

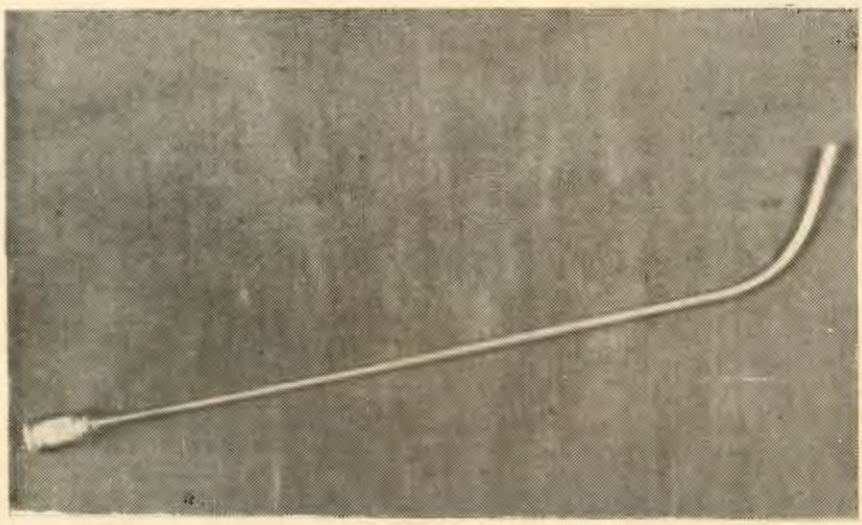

Fig. 1
Cervical mucus canula.

The females of reproductive age, who had married preceding at least 3 years and consumated minimum for 2 years with the husband without using any contraceptive method and had not undergone any hormonal therapy during the last 3 months.

The cases so selected were subjected to a detailed history taking, general examination and gynaecological check-up, routine investigations for sterility for example, basal body temperature, tubal patency test, cervical mucus and endometrial biopsy. Husband's seminogram was also done in every individual.

Three blood samples were collected from every individual in the three different phases of menstrual cycle i.e. one each during proliferative (1-8 days), midcycle (9-15 days) and secretory (16-28 days) phase of the cycle. The blood samples thus collected were centrifuged within one hour and serum was separated and kept at — 20°C until assayed. Radioimmunoassay for FSH and LH was done by Double Antibody Technique.

Observations

The serum LH patterns showed typical midcycle hypersecretion with relatively low concentrations during the proliferative and secretory phase. Mean LH values during the proliferative phase were 23.7 mIU/ml, reached the peak during midcycle (LH values 102.6 mIU/ml) and thereafter showed a decline to 20 mIU/ml in the secretory phase. The serum LH values remained consistently high in cases of primary sterility as compared to normal subjects in control group, though the cases in control group had a similar LH pattern with an LH surge during the ovulatory period. The differences in serum LH concentrations in both groups were statistically significant in all the three phases.

The serum FSH levels showed large variations during the different phases. The mean FSH levels also showed a cyclic pattern but not as marked as LH. The FSH levels were 7.9 mIU/ml and 5.4 mIU/ml during the proliferative and secretory phases of menstrual cycle in sterility cases, respectively, with a peak level during midcycle (31.8 mIU/ml) coinciding with the LH peak. Control cases also exhibited similar patterns, but a little higher FSH values during the proliferative and secretory phases of cycles, but relatively, smaller FSH peak.

The concentration of FSH in sterility cases differed significantly from control cases during all the phases (Table I).

TABLE I

Mean Serum FSH and LH Concentrations in Three Phases of Menstrual Cycles in Primary Sterility and the Control Cases

Phases of the Cycles	Study Group (Primary Sterility)		Control group	
	FSH	LH	FSH	LH
	Mean ± S.D.	Mean ± S.D.	Mean ± S.D.	Mean ± S.D.
Proliferative (1-8 days)	7.9 ± 0.8	23.7 ± 3.7	14.6 ± 2.4	14.7 ± 2.8
Ovulatory (9-16 days)	31.8 ± 3.9	102.6 ± 9.8	26.5 ± 3.6	79.6 ± 6.9
Secretory (17-28/35 days)	5.4 ± 0.6	20.1 ± 2.6	11.2 ± 1.9	13.5 ± 2.0

Statistical Comparison of Mean FSH and LH in Sterility and Control Cases during the Menstrual Cycle

	Proliferative Phase	Midcycle Phase	Secretory Phase
F.S.H.:			
S.E.	0.77	1.34	0.61
t-value	8.64	3.94	9.50
p-value*	.001	.001	.001
L.H.:			
S.E.	1.01	2.82	0.78
t-value	6.93	8.15	8.36
p-value*	.001	.001	.001

* Highly significant.

Out of 30 cases of primary sterility, 7 were anovulatory and 23 were ovulatory. Out of 23 ovulatory infertile females, 3 had tubal blockage, 1 had acutely anteverted uterus and 19 cases with unexplained infertility. All the ovulatory infertile cases showed cyclic changes in FSH and LH concentration within normal range.

Serum FSH values showed variations from phase to phase in ovulatory cycles with definite midcycle peak coinciding the LH surge. The serum FSH, being 8.4 mIU/ml during proliferative phase, rose significantly to 32.8 mIU/ml during midcycle. The follicular stimulating hormone levels declined to 4.5 mIU/ml during the secretory phase of the ovulatory cycles. The changes in FSH concentration were highly significant.

The FSH levels in patients with anovulatory cycles in different phases were higher than ovulatory cycles though not significant statistically and showed cyclic pattern, but not as marked as in ovulatory cycles.

The LH levels showed cyclic pattern in ovulatory cycles with a well marked midcycle peak (50.3 mIU/ml). Comparatively, high LH values were recorded in anovulatory patients without a well difined cyclicity. The LH levels were highly variable from individual to individual.

The levels of LH in anovulatory patients showed a significant difference as compared to ovulatory patients. The cyclic changes in luteinizing hormone concentration were not significant in the former but the latter showed highly significant changes in all the three phases of the cycle (Table II).

TABLE II

Showing Mean FSH and LH Concentrations in Serum During the Three Phases of Ovulatory and Anovulatory Cycles in Cases of Primary Sterility

Phases of Cycle	Ovulatory Cycles		Anovulatory Cycles	
	FSH	LH	FSH	LH
	Mean ± SEM	Mean ± SEM	Mean ± SEM	Mean ± SEM
Proliferative	8.4 ± 0.66	18.5 ± 0.78	17.0 ± 1.50	43.3 ± 1.07
Midcycle	32.8 ± 0.87	50.3 ± 0.93	27.4 ± 1.90	46.6 ± 2.72
Secretory	4.5 ± 0.48	13.6 ± 0.77	17.3 ± 0.95	43.9 ± 1.83

Statistical Comparison of Mean Serum FSH and LH Levels in Ovulatory vs. Anovulatory Cycles

	Proliferative Phase	Midcycle Phase	Secretory Phase
F.S.H.:			
S.E.	5.30	8.49	2.03
t-value	1.62	0.63	6.15
p-value	$>.05$	$>.05$	$<.001$
	N.S.	N.S.	Significant
L.H.:			
S.E.	3.68	16.94	7.76
t-value	6.73	2.07	3.90
p-value	$<.001$*	$<.05$	$<.001$*
		Significant	

* Highly Significant. N.S. = Not Significant.

Discussion

The present study revealed cyclic changes in serum LH and FSH concentrations during the menstrual cycles of primary sterility and control cases with marked midcyclic hypersecretion of LH and FSH. Relatively low levels were measured during proliferative and secretory phases.

The serum LH levels in primary sterility cases showed fluctuating patterns but with a single, sharp and significant LH peak (mean LH 102.6 mIU/ml) during the midcycle, coinciding with ovulation time. Relatively low concentrations were observed during the proliferative (mean LH 23.7 mIU/ml) and secretory phase (mean LH 20.1 mIU/ml) serum LH being slightly high in proliferative phase as compared to latter. The difference in serum LH concentration during different phases was statistically significant. The overall cyclic changes in the serum LH concentrations in infertile females compared fairly well with the serum LH patterns in control cases. The most consistent finding was occurrence of LH peak during the midcycle in both the groups. The control cases exhibited nearly similar cyclic changes in serum LH levels with single well marked and significant LH peak (mean LH 79.6 mIU/ml) and relatively low levels during proliferative (mean LH 14.7 mIU/ml) and secretory phase (mean LH 13.5 mIU/ml), the levels being slightly high during proliferative phase. The serum LH levels showed statistically significant changes in all phases of cycle.

Several other investigators namely, Midgley and Jaffe (1966), Taymor *et al* (1968), Midgley and Jaffe (1968 and 1971), Abraham *et al* (1972), Wide *et al* (1973) and Thorneycroft *et al* (1974) have investigated the variations in serum levels of LH and FSH during menstrual cycle. There was a good agreement of our findings to these authors' findings. A distinct midcycle LH peak was observed in their respective studies. In most of these studies higher LH levels were found during the follicular phase than during the latter part of luteal phase of the cycle.

The serum FSH and LH patterns showed recognisable difference during anovulatory and ovulatory cycles.

Typical midcycle LH peak was observed along with low follicular and luteal levels. In contrast, the LH patterns during anovulatory cycles showed relatively higher LH values but without a well-defined cyclicity. The serum LH levels practically showed no or little fluctuation during the different phases of menstrual cycle. The difference between midcycle LH values and follicular values, and midcycle and luteal LH values, was very minor and far from any significance. Apart from it, the LH levels were highly variable from individual to individual.

Serum FSH levels exhibited a distinct cyclicity in the ovulatory cycles. There was a distinct midcycle peak (mean FSH 32.8 mIU/ml) with comparatively low levels during follicular (mean FSH 8.4 mIU/ml) and luteal phase (mean FSH 4.5 mIU/ml) of the cycle. Contrary to this, anovulatory cycles, lacked the cyclicity in serum FSH levels, however, there was a rise in mean FSH levels to midcycle.

Summary

Serum LH and FSH concentrations showed cyclic and periodic changes during the proliferative midcycle and secretory phase of the menstrual cycle. The serum LH hormone values remained consistently high in cases of primary sterility as compared to normal subjects in control group, however, the latter exhibited similar LH pattern with a typical peak. Serum follicular stimulating hormone levels showed large variations during the different phases, though it showed cyclic pattern but not as marked as serum LH. The serum FSH and LH levels were comparatively high in anovulatory patients but lacked in typical cyclicity and LH surge as the ovulatory cycles. These high values were statistically highly significant. The changes in serum LH concentrations during different phases of anovulatory cycle were insignificant in contrast to significant variations in ovulatory cycles.

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