EFFECT OF PROSTAGLANDIN E₂* ADMINISTRATION ON THE MALE REPRODUCTIVE SYSTEM:
A BIOCHEMICAL AND CYTOMORPHOLOGICAL STUDY**

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ABSTRACT
Prostaglandin E₂ (PGE₂) treatment of adult male rats altered the functional integrity of testis and accessory sex organs as reflected by changes in the estimations of the alkaline phosphatase, acid phosphatase, succinic dehydrogenase in tests, sialic acids in epididymis, citric acid in seminal vesicles and fructose in prostate. The wet weights of testis and accessory sex organs showed a slight decrease, while insignificant increase was noticed in the weight of pituitary. Histologically, prostaglandin produced marked decrease in the sperm count and increase in the number of exfoliated immature spermatozoa in epididymis. The results suggest that the changes in reproductive parameters might be a consequence of endocrinological and functional disturbances induced by PGE₂.

INTRODUCTION
Prostaglandins (PG's) play a physiological role in the hypothalamic control of gonadotropin secretion, is well established. Direct evidence has also been obtained to the involvement of prostaglandin in the release of LH. Administration of PGE₂ and PGF₂α was effective to reduce LH levels. Chronic treatment with prostaglandin produced marked decrease in spermatogenesis, atrophy of testis and accessory sex organs and decrease in plasma testosterone level. The goal of present research was (i) to demonstrate changes produced in biochemical constituents of testis and accessory sex organs and (ii) study of cytomorphological alteration induced by the treatment of i.m. injections of PGE₂ for 15 days.

EXPERIMENTAL
Adult male albino rats (Holtzman strain) weighing approximately 200 g were used for the present investigation. Rats were kept in well-ventilated room with standard light and dark periods and were fed with synthetic feed pellets (Hindustan Levers, Bombay) and water ad libitum. The rats were weighed and divided into two groups of 12 animals each. Prostaglandin E₂ (2 mg/kg b.wt.) was administered i.m. in rats, once daily, for 15 days. Control group was sham-treated with 10% ethanolic saline.

The animals were sacrificed by decapitation and testes, epididymis, seminal vesicles, prostate and pituitary glands were excised. The wet weights of the organs were taken (Table I) and small pieces of testis, epididymis and pituitary were fixed in Bouin's fixative for histological study.

Acid (ACP) and alkaline phosphatase (ALP) and succinic dehydrogenase (SDH) were determined in the testis by the techniques of Shinowara et al. and Kun and Abood respectively. The amount of sialic acids in caput and cauda was measured separately by thiobarbituric acid assay of Waran. Fructose content in prostate and citric acid in seminal vesicles was determined by the methods of Mann and Linder and Mann respectively. The values are statistically analysed and presented in Table I. For histological study, testis, epididymis and pituitary gland were fixed in Bouin's fluid for 24–28 hours, washed with 70% alcohol, dehydrated, cleared in xylene, impregnated, the paraffin sections were cut at 7 μ and stained with Eosin-Haematoxylin stain. In order to differentiate different cells in pituitary, differential stain was used.

RESULTS AND DISCUSSION
On PGE₂ administration, no change in body weight and considerable regression was seen in the wet weight of testis and seminal vesicles (p < 0.05), while only slight decrease in that of epididymis and prostate. However, the weight of pituitary showed a slight increase in comparison to control (Table I). Administration of PGE₂ produced a marked change in the orientation of the seminiferous tubules (Fig. 1A, 1B). Various stages of spermatogenesis were dislocated from their site with a marked reduction in the number of spermatozoa (Fig. 1B). In some of the tubules, immature cells were migrated from the periphery to the lumen of the seminiferous tubules along with spermatozoa. Leydig cells were well developed showing normal orientation. The epididymis of PGE₂ treated animals showed an increase in the number of exfoliated immature germ cells in the lumina of ductuli of caput as well as cauda epididymis (Fig. 2B), while the number of spermatozoa significantly decreased. The epithelial linings of the ductuli of caput as well as cauda epididymis were proliferated (Figs. 2B, 3B) as compared to that of control. In pituitary, an increase in the size and number of granulocytes (Fig. 4B) was observed.

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*** For reprint requests.
### Table I

**Effect of prostaglandin E₂ (PGE₂) on biochemical composition of testis and accessory reproductive organs**

Values are mean ± S.E. for twelve animals in each group. Values in parentheses represent the wet weights of respective organs in mg per 100 g body weight.

<table>
<thead>
<tr>
<th>Animal</th>
<th>Testis</th>
<th>Epididymis</th>
<th>Prostate</th>
<th>Seminal vesicles</th>
<th>Pituitary mg/g</th>
</tr>
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<tbody>
<tr>
<td></td>
<td>ACP (mg of PO₄ released/g)</td>
<td>ALP (µg of PO₄ liberated/g)</td>
<td>SDH (µg of dye reduced/g)</td>
<td>Caput Sialic acids (mg/g)</td>
<td>Cauda Sialic acids (mg/g)</td>
</tr>
<tr>
<td>Vehicle-treated</td>
<td>9.3 ± 0.7 (986 ± 106)</td>
<td>6.2 ± 1.2</td>
<td>526 ± 0.161.0</td>
<td>0.0732 ± 0.002 (333 ± 30)</td>
<td>0.0617 ± 0.001</td>
</tr>
<tr>
<td>PGE₂-treated (2 mg/kg b.wt. for 15 days)</td>
<td>9.4 ± 1.0 (828 ± 69)*</td>
<td>6.29 ± 0.1</td>
<td>381 ± 0.92.3</td>
<td>0.1037 ± 0.002* (327 ± 20)</td>
<td>0.105 ± 0.001*</td>
</tr>
</tbody>
</table>

* p < 0.05 in both control and treated.
The histological observations on tests suggested that the effect of PGE₂ is both quantitative as well as qualitative. The observed decrease in spermatogenesis and such earlier reports⁵ may either be due to direct action of PGE₂ on germinal epithelial cells of seminiferous tubules¹⁴ or by inhibition of androgen secretion in Leydig cells thus altering the specific receptor sites¹⁵. The dislocation of various spermatogenic stages may be due to testicular contraction and/or may be caused by altering testicular hemodynamics. Slight decrease in the weights of accessory sex organs was, perhaps, the manifestation of altered testicular activity⁶,

Fig. 1A–4B. Fig. 1A. Control testis showing full spermatogenesis (× 100). Fig. 1B. Treated testis with dislocated spermatogenic stages (× 100). Fig. 2A. Control caput epididymis with lumen full of sperm (× 100). Fig. 2B. Treated caput epididymis with lumen containing exfoliated immature cells (× 100). Fig. 3A. Normal cauda epididymis (× 100). Fig. 3B. Treated cauda epididymis (× 100). Fig. 4A. Control pituitary (× 400). Fig. 4B. Treated pituitary with increase in the size and number of granulocytes (× 400).

Statistical significance with PGE₂ was seen in concentrations of SDH, citric acid and fructose (p < 0.05). There was marginal increase in ACP and ALP of tests and that of sialic acid in caput and cauda epididymis statistically significant (p < 0.05). Increase in the activity of ALP and ACP in the present studies might be responsible for the increased phagocytotic activity of the tubules and this may be attributed to decrease in the weight of testis while the reduction in SDH might be due to severe regression and metabolic disturbance in tests⁶. Increase in sialic acid concentration in caput as well as cauda epididymis might be due to its decreased utilization required for maturation of spermatozoa. The decrease in prostatic weight and fructose level after PGE₂ administration is probably due to androgen deprivation of prostate as formation of fructose in male sex organs is hormone dependent¹¹. The observed decrease in citric acid may also be attributed to insignificant decrease in testosterone level. An increase in weight of pituitary might have been due to stimulatory effect of PGE₂ on gonadotropin release as is evident from the size and number of granulocytes.

Thus, the administration of PGE₂ altered the structural and functional integrity of the testis and accessory sex organs as evident from biochemical and cytomorphological changes. These may not reflect the direct actions, but could be a consequence of other endocrinological and/or functional changes induced by PGE₂. The occurrence of higher incidence of immature spermatozoa and reduction in sperm number particularly from epididymis strongly implicates that PGE₂ caused sterility.