CHAPTER VII

EARLY INFLUENCE OF TESTOSTERONE PROPIONATE ADMINISTRATION TO NORMAL INTACT MALE ALBINO RATS (*Rattus norvegicus albinus*) ON CERTAIN ASPECTS OF HEPATIC METABOLIC PATTERNS : IV ASCORBIC ACID CONTENT

Ascorbic acid (AA-Vitamin-C) is synthesized in the hepatic tissue of mammals except in man and monkey. It plays an important role in cellular oxidation reduction processes, apart from its usual role as a vitamin (Meikle Jhon, 1953). This function of AA in recent years is being increasingly studied with respect to different tissues and under varied conditions (Mapson, 1953; Goodwin, 1960; Ramchandran *et al.*, 1975; Ambadkar and Gangaramani, 1981). It is also evident (Stubbs and Mckernan, 1967; Stubbs *et al.*, 1967), that the testicular hormones significantly influence the tissue AA levels in male rats. Further, dynamic interrelationship between AA and circulating level of testosterone has also been suggested (Chinoy and Parmar, 1975). Involvement of AA in steriodogenesis is well established (Szent, 1957; Bacq and Alexander, 1961; Biswas and Deb, 1970; Chinoy, 1972a, b; Chinoy and Seethalakshmi, 1978). Alterations in AA content have also been reported under variety of experimental conditions such as hypophysectomy, adrenalectomy, gonadectomy etc. Salmon and Stubbs (1961) showed reduced AA synthesis after hypophysectomy,

Nathani et al. (1971) observed increased AA utilization in liver and kidney after adrenalectomy in rats, and Chinoy and Rao (1979) reported depletion of hepatic and adrenal concentration of AA after gonadectomy. Moreover Rush and Kline (1941), Banerjee and Ghosh (1947), Mazur et al. (1961) and Banergee and Ganguli (1962) have suggested involvement of AA in various metabolic activities. There is enough experimental evidence showing that deficiency of AA leads to disturbances in carbohydrate, lipid, protein and iron metabolism.

According to Ambadkar and Gangaramani (1981), the AA levels in the hepatic tissue registered significant rise after castration and showed a time dependent fall after the initial increase. They also observed that replacement therapy in case of 24 hour castrates led to results contrary to expected reparative effect of androgen administration (Ambadkar et al., 1987). Against this background, it was thought necessary to investigate the immediate influence of exogenously administered testosterone propionate in normal intact healthy albino rats.

MATERIAL AND METHODS :

Adult male albino rats Rattus norvegicus albinus selected for the present study fell within a weight range of 120-160 gms, maintained on a balanced diet and water ad libitum. Normal intact animals were administered with a

single intramuscular (i.m.) injection per animal of testosterone propionate in the following three different doses viz.-0.1, 0.25 and 0.5 mg. and were sacrificed at 30, 60, 90 and 120 minutes after hormone administration.

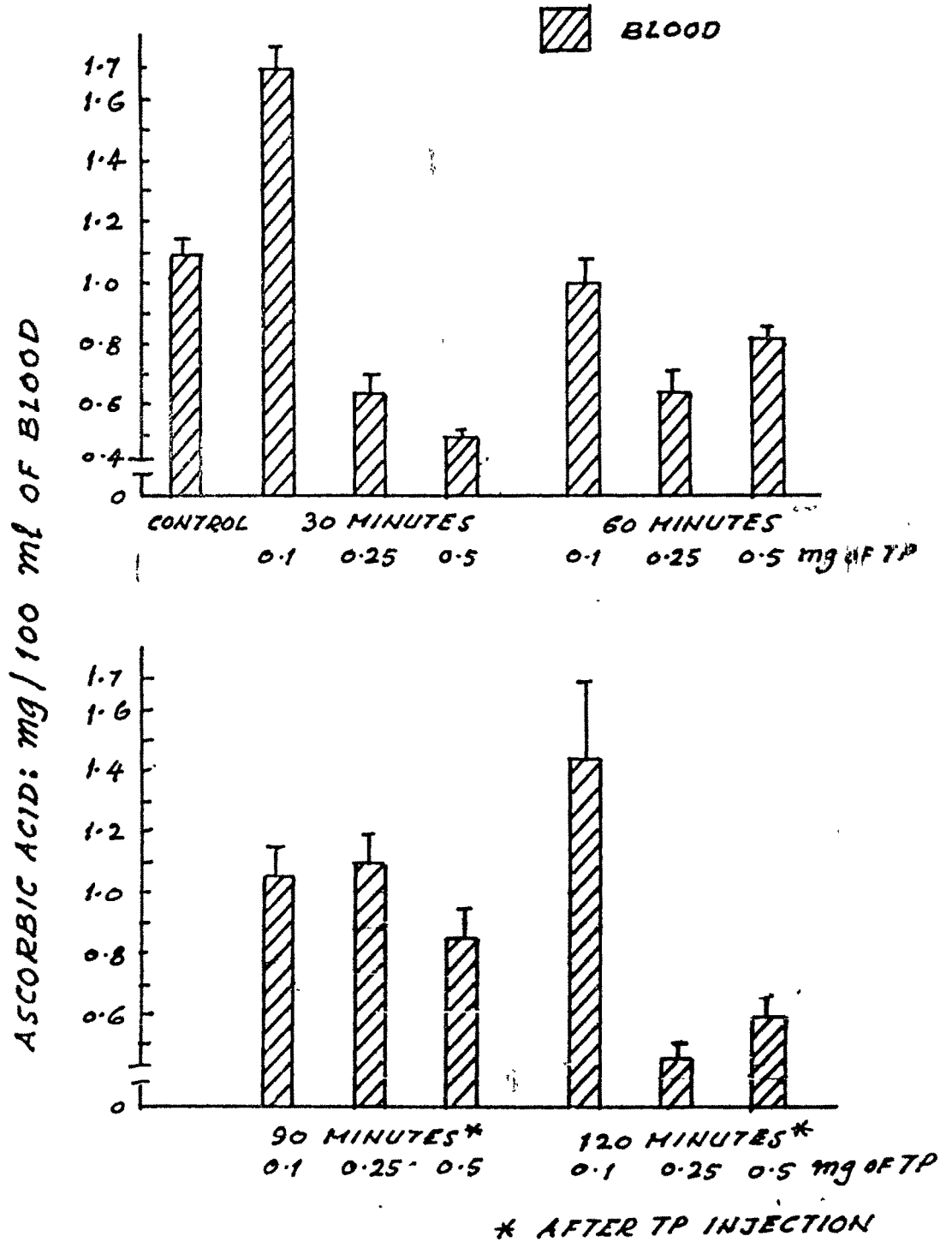
Blood was collected from jugular vein in pre-heparinized test tubes, and was assayed for AA content. Later, the animals were dissected out and hepatic tissue from the median and Spigelian lobe was taken out and processed separately for AA content as per the method described in Chapter-1.

RESULTS :

The results obtained during the present study are represented in Table 7.1 and Figures 7.1 and 7.2.

Administration of 0.1 mg of TP to normal intact males led to significant reduction in the Ascorbic Acid content of the liver lobes. This was obvious within 30 minutes of injection and remained at more or less the same level upto 90 minutes but by 120 minutes further deplition was evident. In contrast, the blood AA level indicated a slight increase initially within 30 minutes but at 60 and 90 minutes intervals reduction was evident. Later, recovery was evident.

BLOOD ASCORBIC ACID CONTENT (AA)



HEPATIC ASCORBIC ACID CONTENT (AA)

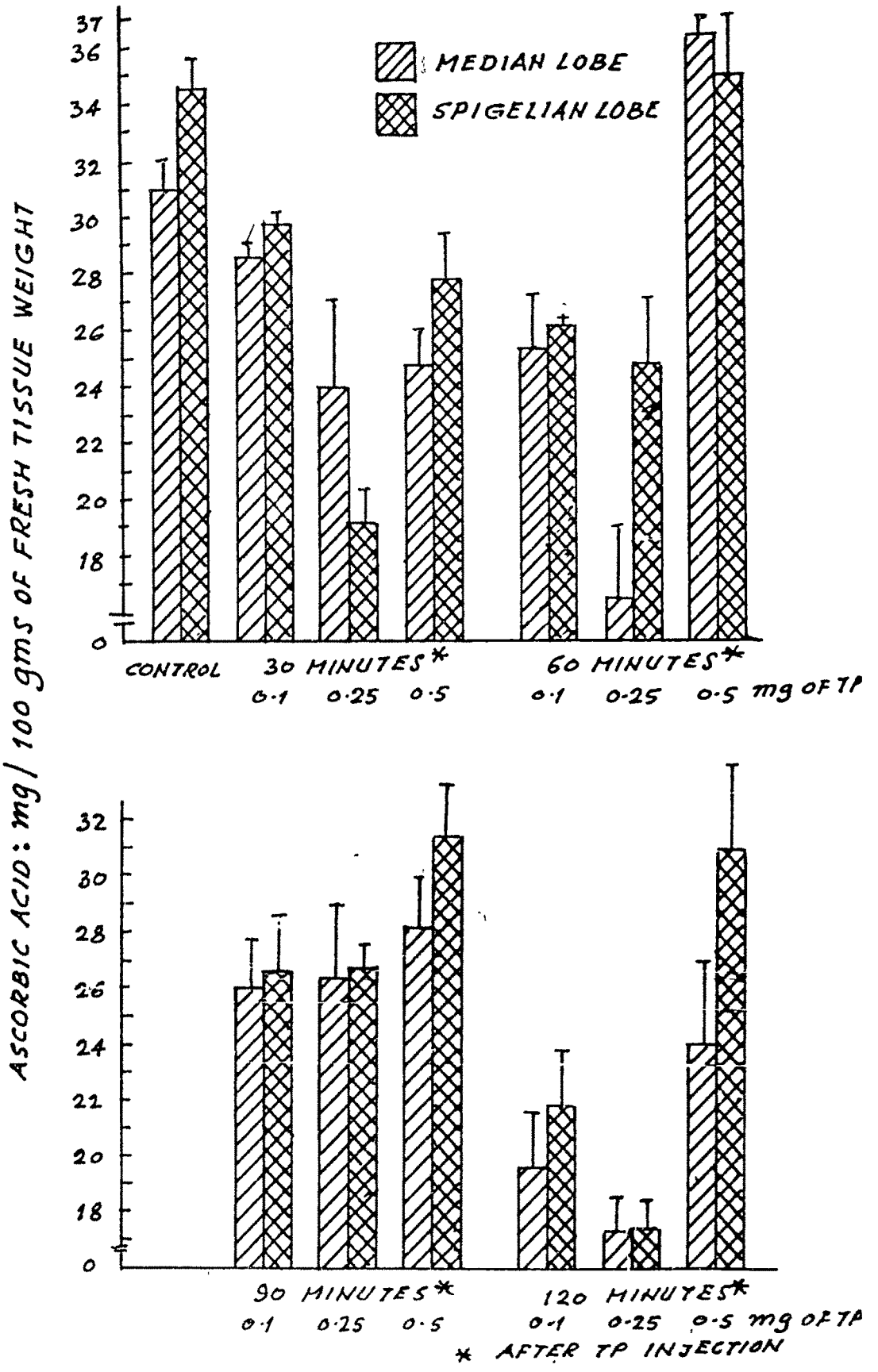


Table 7.1 : Ascorbic acid content of hepatic tissue and blood under influence of TP administration to normal rats

Post operative intervals	Normal animal injected with TP								
	0.1 mg			0.25 mg			0.5 mg		
	Blood	M	Sp	Blood	M	SP	Blood	M	SP
30 minutes	1.68 ± .30	28.70 ± .24	29.80** ± 0.33	0.62***** ± .07	24.08*** ± 3.4	19.20***** ± 1.4	0.50***** ± .02	24.98*** ± 1.37	27.90*** ± 1.7
60 minutes	0.99 ±0.09	25.42** ± 2.73	26.23**** ± 0.02	0.65***** ± .07	16.53***** ± 2.4	24.97***** ± 2.3	0.82* ± .04	36.35 ± 4.0	35.60 ± 3.0
90 minutes	1.06 ±0.12	26.00** ±1.831	26.79*** ± 2.68	1.1 ±0.1	26.23** ± 2.6	26.80***** ± 0.7	0.86* ± .09	28.13*** ± 2.1	31.45 ± 2.4
120 minutes	1.45 ±0.22	19.64***** ± 1.98	21.83***** ± 2.18	0.47***** ±0.06	17.12***** ± 1.3	17.31***** ± 1.70	0.61***** ±0.05	24.08*** ± 3.1	31.12 ± 3.53

Normal ascorbic acid content mg/100 gms of tissue or mg/ 100 ml of blood

Blood	M (Hepatic tissue median)	Sp (Spigelian lobe)
1.16 ± 0.23	31.66 ± 3.02	34.53 ± 3.33

* P < .05 ** P < .01 *** P < .005 **** P < .001 ***** P < .0005

± S.E.M. of at least eight animals.

With 0.25 mg dose of TP the Ascorbic Acid content of both the lobes showed greater depletion, within 30 minutes of hormone administration. At 60 minutes the median lobe AA content decreased further whereas Spigelian lobe level showed improvement. By 90 minutes further improvement was observed, though the level was still sub-normal. By 120 minutes a marked and sudden reduction was noticed (approx. 50% of normal values).

Higher dose 0.5 mg TP injection caused reduction in AA by 30 minutes which was found to recover to normal level by 60 minutes in both the lobes. The median lobe once again indicated a gradual depletion by 90 and 120 minutes, while the Spegelian lobe exhibited subdued levels.

The blood AA level showed depletion after administration of 0.25 and 0.5 mg within 30 minutes and no sign of recovery was noticed even at 120 minutes, however, a transitional increase in the blood AA content at 90 minutes was observed after only 0.25 mg TP dose.

DISCUSSION :

In view of the importance of hepatic gland in the over all metabolism of the body it is quite likely that certain factors such as age and diet influence its function. These are known to influence AA metabolism (Ehmke, 1956).

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Age and diet of the experimental animals, therefore, were kept constant throughout the present investigation. Thus the changes noted could be attributed to the experimental treatment employed.

Depletion in the AA content after few weeks of orchidectomy has been reported by several workers (Stubbs and Mckernan, 1967; Stubbs et al., 1967; Khandwekar et al., 1973 and Muddashwar et al., 1984), and was thought to be due to deficit of testosterone. Contrary to this idea our earlier findings (Ambadkar and Gangaramani,1981; Ambadkar et al., 1987) indicated an increase in AA content within 24, 48 hours after gonadectomy. As against this significantly sub-normal levels of AA could be observed, within an hour of replacement with TP.

It is, therefore, apparent that early response to hormonal disturbances are markedly different from those observed by several workers, who had allowed a time lapse of one to few weeks after gonadectomy as well as after hormonal replacement.

In the light of this, as stated earlier, it was thought desirable to investigate the immediate hepatic response of intact animals to exogenous administration of TP. Results obtained here indicated reduction of hepatic AA levels within first 30 minutes of hormone administration. With further time lapse, the pattern of fluctuations noticed

in the blood as well as hepatic AA levels amply indicated that even slight elevation of titres of circulating androgens would also lead to undesirable alterations in AA metabolism. The sole exception was obvious recovery only in the case of hepatic AA level (at 60 minutes interval after 0.5 mg TP dose) though, here also blood AA level was distinctly very low.

In this connection reference to the recent work of Muddeshwar et al. (1984) is of interest. They have reported that testosterone and other androgenic compounds exert a depressor-type of action at gene level, after being subjected to 5- α reductase action in the cytosol, and thereby influence production of specific mRNAs. These authors have shown that an important AA synthesizing enzyme and catabolizing enzyme are reciprocally affected by replacement therapy and orchidectomy respectively.

Taking into consideration the findings of Muddeshwar et al. (1984) and on the basis of results of present study, it could be said that alterations in circulating testicular androgen levels exert a regulatory effect on the rate of AA synthesis as well as its degradation/retension in the hepatic tissue. Exogenous TP injection brings about either reduction of hepatic AA synthesis or increases its rate of intrahepatic as well as peripheral utilization. This statement is borne well by

the present study where decreased hepatic AA levels were obtained after exogenous administration of TP.

It is, therefore, suggested that the hepatic mechanism of AA synthesis and that of its retention are influenced in different ways and probably independently of each other.