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THE POSTOPERATIVE DECREASE OF PLASMA TESTOSTERONE IN MAN, AFTER MAJOR SURGERY, IN RELATION TO PLASMA FSH AND LH*

HANS CARSTENSEN†, BIRGITTA AMÉR, INGVAR AMÉR and LEIF WIDE

Department of Physiology, Umeå University Medical School, Umeå; Department of Anaesthesiology, The Hospital, Oskarshamn; and Department of Clinical Chemistry, The University Hospital, Uppsala, Sweden

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SUMMARY

Confirmation was obtained of the pronounced postoperative decrease of plasma testosterone in the human male. Testosterone levels were determined using a competitive protein binding assay after one paper chromatographic step. After different types of major surgical operation, in 8 patients, a nadir in the testosterone concentration (sample taken at 9 a.m.) was found on the first postoperative day (127 ± 84 S.D. ng/100 ml, compared to controls of 782 ± 259 ng/100 ml) and on the second postoperative day (136 ± 73 ng/100 ml). The decrease was still significant on days 5 and 6 ($p < 0.01$) but not on days 9–11. A low plasma testosterone concentration was found (in a sample taken at 3 p.m.) in a patient with a 6 day history of a haemorrhaging gastric ulcer which perforated 6 h earlier (182 ng/100 ml). The mean control values of the patients did not differ significantly from those of ten healthy male medical students (775 ± 332 S.D. ng/100 ml). After a 30 min workout on a bicycle ergometer, the plasma testosterone levels of the latter were unchanged (821 ± 392 ng/100 ml).

No change in immunoreactive plasma LH, as measured in the same blood samples used for testosterone determinations, occurred after surgery, nor was any change noted in FSH levels, except in the cross-sectional study where a decrease occurred on day 2. It was concluded that neither gonadotropic hormone was responsible for the decreased level of testosterone.

INTRODUCTION

PLASMA testosterone levels were shown by Carstensen *et al.* [1–3] and by Matsumoto *et al.* [4] to decrease, after major surgery in human male subjects. In the absence of concomitant changes of plasma LH [3, 5] it was not possible to explain this decrease as a result of a decreased pituitary LH stimulation although Charters *et al.* [6] reported a small decrease of plasma FSH and LH shortly after surgical operations. Since, however, the control mechanism for testosterone secretion may involve FSH and possibly other pituitary hormones in addition to LH [7], we decided to study the relationship between plasma LH, FSH and testosterone, particularly during the first days and weeks after some major surgical operations. One reason for this was the recent demonstration by Faiman and Winter [8] that the diurnal variation of plasma testosterone was related to a diurnal variation of FSH and that both were uninfluenced by dexamethasone administration, while LH showed no diurnal variation and was increased after minor surgery [4]. Carstensen *et al.* [3] previously showed that administration of

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†Requests for reprints: Department of Physiology, Umeå University, S 90187 Umeå 6, Sweden.

cortisone acetate to a human volunteer, for 3 days, failed to influence the plasma testosterone concentration, at least to any great extent. Since ACTH has been shown to lower plasma testosterone [9, 10] the ACTH activation mechanism may have some, as yet poorly understood, effect on the plasma testosterone concentration.

In earlier work from this laboratory a double isotope derivative method was used to determine testosterone [3]. It tended to give values too high to be possible due to an isotope effect when the derivative was purified by repeated chromatography. These difficulties have been overcome in the present work by applying a modified competitive protein binding method (CPB).

We have also investigated whether physical exercise exerted any effect on the plasma testosterone concentrations, in view of its effect on human growth hormone, which is also affected by major surgery [11, 12] although this effect is of short duration and may be over by the time the operation is finished [6, 13].

MATERIALS AND METHODS

Subjects. Blood specimens were obtained from eight patients undergoing surgery at the Oskarshamn hospital surgical clinic. The blood specimens were obtained by venepuncture at $9{\cdot}00 \pm 0{\cdot}30$ h and collected in heparinized glass centrifuge tubes. All subjects were evaluated clinically to rule out any endocrinopathies and abnormalities of major bodily functions, in particular of the liver and kidneys. Subject VII obtained the cytostatic agent, cyclophosphoramide (Sendoxan^{R}, Pharmacia), 400 mg i.v. daily on days 0–9. This treatment did not seem to influence the plasma concentrations of testosterone, FSH or LH. One patient (No. VIII) received Furadantin, 150 mg daily, perorally from day 14 after the operation because of a urinary infection. Furadantin has been shown to be an antispermatogenic agent and a stimulus of the pituitary gonadotropin secretion and of testicular testosterone secretion in rats [14, 15]. Since it was given late during the period of this study, it does not affect the conclusions drawn in this paper. The blood specimens were centrifuged at 1000 rev./min for 15 min at room temperature within 1 h of collection. Duplicate samples of 2 ml of plasma were added to glass tubes containing 12,000 d.p.m. of [1, 2-^{3}H]-testosterone. One ml samples were transferred to clean, empty glass tubes for LH and FSH determinations. Ten ml samples were taken for determination of testosterone binding activities to be reported in a separate communication. All plasma samples were stored at −20°C or below until used.

Blood specimens were likewise obtained from 10 healthy medical students before and 10–20 min after exercise for 30 min on an ergometer bicycle. The initial load was 400 kpm for 10 min, then 700 kpm for 10 min and finally 1000–1200 kpm for 10 min to reach a pulse rate of between 170–180 per min. These blood specimens were centrifuged at 11,500 rev./min for 20 min in a Sorvall RC2-B centrifuge at 4°C. Duplicate 2 ml plasma samples were added to tubes containing 7500 dpm of 1, 2-^{3}H-testosterone and immediately extracted.

Immunoreactive FSH and LH in plasma were assayed by a radioimmunosorbent technique [17, 18]. LH in plasma was measured by utilizing human pituitary LH [16] labelled with ^{125}I and rabbit anti-human pituitary LH antibodies. The LH preparation had a biological activity of 14000 IU (2nd IRP-HMG) per mg. The results were expressed in ng/ml. One ng of LH was equivalent to 83 ng of LER-

907 in the immunoassay. FSH in serum was measured by utilizing human pituitary FSH[16] labelled with ^{125}I and guinea-pig antihuman pituitary FSH antibodies. The FSH preparation had a biological activity of 14000 IU (2nd IRP-HMG) per mg. The results were expressed in ng/ml. One ng of FSH was equivalent to 369 ng of LER-907 in the immunoassay. In the radioimmunoassays the standards were dissolved in plasma with undetectable levels (less than 0·3 ng/ml) of the hormones to be assayed. The samples were assayed in duplicate and the results were calculated by the use of a logit transformation as proposed by Rodbard *et al.*[19].

Testosterone CPB. [1,2-^{3}H]-testosterone (SA 51 Ci/mmol), obtained from New England Nuclear, was purified by thin layer chromatography and paper chromatography and used after determining its homogeneity (> 94%). Aliquots were added to glass tubes using an automatic pipetting device (pipetting error 4·1%) and used for the series of patient. Later on this method was abandoned and the steroid pipetted with a 50 μl Carlsberg pipette (pipetting error 0·1%). This addition of ^{3}H-testosterone was employed to monitor procedural losses. Pregnancy plasma was obtained from one woman during the last pregnancy month and used throughout this study as a source of testosterone binding protein. One ml aliquots were stored at −20°C in sealed ampoules. One ampoule was thawed and diluted with 100 ml of 0·1 M phosphate buffer, pH 7·2. [^{3}H]-testosterone, $3{\cdot}5 \times 10^6$ d.p.m., was dissolved in this solution which was then stored at 3°C and used over a maximum period of one month.

Two ml plasma aliquots were extracted three times with 5 ml of chloroform, A.R., Merck-Darmstadt. The combined chloroform extracts were washed with 1 ml of 0·1 N NaOH, then twice with 2 ml of deionized, quartz-distilled water and evaporated to dryness under a stream of nitrogen in a waterbath (40°C). The extracts were then transferred to paper chromatograms using diethyl ether (UVASOL, Merck)-acetone (Fisher A.R.) 1 : 1 v/v, 100 μl × 5. Whatman No. 1 filter paper, cut into 2 cm wide lanes, was used. This was purified by Soxhlet extraction in the following series of solvents, deionized and redistilled water, absolute ethanol and redistilled n-hexane. Paper chromatography was carried out in a Bush A system, heptane (Fisher A.R.) 500, methanol (Merck A.R.) 425, and water (deionized and quartz-distilled) 75, for defatting. The chromatogram was then dried and rechromatographed in a Bush B3 system, redistilled benzene 170, redistilled n-hexane 330, methanol 400 and water 100. The areas corresponding to testosterone were eluted with 7 ml of methanol (Merck, A.R. or Fisher, A.R.). By this procedure testosterone was separated from most steroids which might interfere in the CPB assay [cf. 20], e.g. estradiol-17β and 5α-dihydrotestosterone. Two ml distilled water samples were also carried through the procedure as blanks.

Duplicate samples of the purified plasma extracts were then assayed for testosterone using a CPB method[21]. Results were calculated in ng per 100 ml of plasma using a program written for the Hewlett–Packard Model 9810A calculator.* The reproducibility of the standard curve, plotted as per cent bound vs. ng testosterone, is illustrated in Fig. 1.

*The authors wish to thank Mr. G. Westling cordially for writing this programme and for valuable advice.

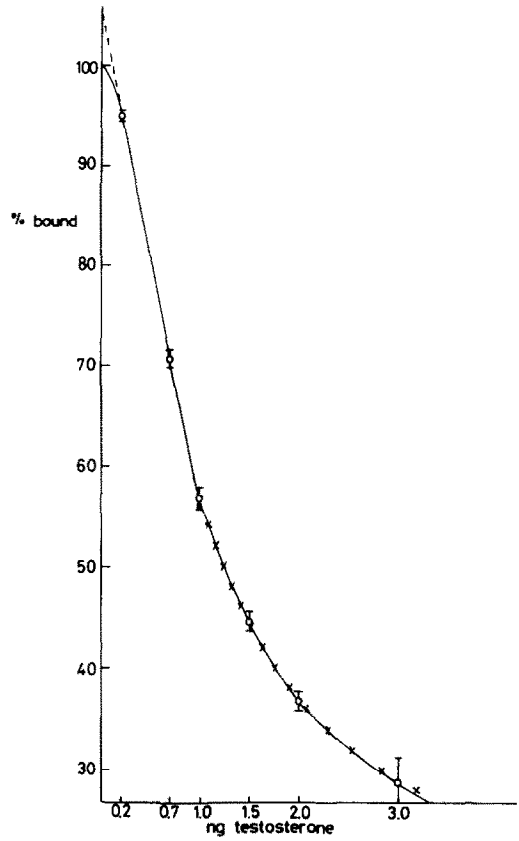

Fig. 1. Competitive protein binding of standard testosterone (circles ± 2·5 S.E. connected by solid line) fitted to a straight line equation between 0·2 and 1 ng ($y = 104{\cdot}3 - 47{\cdot}7x$) and to a parabolic equation between 1 and 3 ng ($1/(y - 11) = 0{\cdot}0048 + 0{\cdot}0169x$), as represented by crosses in the figure (cf. Leclercq R., Täljedal L. -B. and Wold S.: *Clin. chim. Acta* **36** (1971) 257). Deviation from computed curve was 0·01 ng (1·0%) for x = 1 ng, 0·02 ng (−1·36%) for x = 1·5 ng, 0·01 ng (0·48%) for x = 2 ng and 0·0003 ng (0·01%) for x = 3 ng.

RESULTS

Effect of exercise. The mean concentrations of plasma testosterone in 10 healthy male students, age 20–27, before and after a bicycle ergometer work load, carried out shortly after noon, are listed in Table 1. The post exercise sample was taken 10 min after exercise was stopped, except for the last four subjects listed where the time lag was 20 min. A paired t-test revealed no difference between the groups, nor was there any difference in plasma testosterone concentrations before and after exercise. Variation between duplicate plasma specimens was 18%.

Effects of surgical operations. The main data concerning the eight male patients undergoing surgical operations are summarized in Table 2. Four patients (III–VI) underwent partial ventricular resection. Two patients obtained spinal anaesthesia (I and II), all the others obtained general anaesthesia induced by barbiturate i.v. and endotracheal intubation using a muscle relaxant followed by halothane and nitrous oxide. No preoperative specimen was obtained from patient II who was brought to the hospital after a traffic accident. The preoperative plasma

Table 1. Plasma testosterone concentrations of healthy male medical students before and after exercise, 10–20 min after running a bicycle ergometer for 30 min at a maximal load of 1200 kpm and a pulse frequency of 170–180 per min

Age	Before work	After work	(min)
27	1546	1594	(10)
22	905	1264	
25	500	474	
24	924	756	
24	736	1023	
20	666	704	
21	654	603	(20)
23	503	474	
23	384	348	
21	934	972	
mean	775	821	
S.D.	332	392	
Paired t test	N.S.		

Table 2. Data concerning the patients undergoing surgery

		Age	Diagnosis	Operation	Anaesthesia
Subject	I	42	Hernia disci intervertebralis	Laminectomy	Intradural spinal
	II	17	Leg fracture (tibia + fibula + femur)	Reposition + Küntschner nail	Intradural spinal
	III	53	Perforated gastric ulcer	Partial ventricular resection	Narkotal^R Celocurin^R Fluothane^R + N_2O
	IV	30	Gastric ulcer	Partial ventricular resection	Fluothane^R + N_2O
	V	38	Gastric ulcer	Partial ventricular resection	Fluothane^R + N_2O
	VI	33	Duodenal ulcer	Partial ventricular resection	Fluothane^R + N_2O
	VII	54	Hypernephroma with metastases	Unilateral nephrectomy	Fluothane^R + N_2O
	VIII	52	Carcinoma of the colon	Extirpation + Colostomy	Fluothane^R + N_2O

Narkotal, Astra: Enibomalum (5-(2-bromoallyl)-5-isopropyl-1-methyl-barbituric acid) + Phenazonum (1-Fenyl-2, 3-dimethyl-pyrazolone-(5).

Celocurin^R, Vitrum: Suxamethonum (2, 2'-Succinyl-oxy-bis (ethyltrimethyl ammonium-hydroxide) chloride).

Fluothane^R, Scanmeda: Halothane 100 *g* (2-Bromo-1,1,1-trifluoro-2-chloroethane) + Thymol 10 mg.

testosterone concentration was markedly low in patient III who had a haemorrhaging gastric ulcer which perforated about 6 h before the sample was taken. This patient had a 6 day history of haematemesis but no circulatory shock symptoms. He underwent gastroscopy under local anaesthesia when the ulcer perforated. The preoperative sample was thus in this case taken in the afternoon just before the gastrectomy. In the cross-sectional study shown in Table 3 the control values of subjects II and III were obtained 8 weeks after the operation.

Table 3. Plasma testosterone concentrations of male patients after a major surgical operation

			Days after operation							
		Control*	1	2	5–6	9–11	13–14	17–19	21–22	25–57
Subject	I	623	243	247	621	669	647	686	813	
	II	846†	50	36	145	320	436	552	837	846
	III	590‡	142	200	638	643	703		770	590
	IV	813	83	82	242	676	545			776
	V	353	34	100	260	216	349	316	638	
	VI	1133	63	174	853	1206	1044			1728
	VII	810§	252	178	378	417	634		652	711
	VIII	1090	151	74	185	287	378	722	687	
Mean		782	127	136	415	554	592	569	733	930
S.D.		259	84	73	258	321	225	184	85	456
P value			< 0·001	< 0·001	< 0·01	N.S.	N.S.	N.S.	N.S.	N.S.

*The concentration at the day of or the day before the operation if not otherwise stated.

†Leg fractures. The value obtained 56 days after the operation used as control.

‡Perforated ventricular ulcer with low testosterone concentration on the day of admission to the hospital, being 182 ng/100 ml. The value obtained 57 days after the operation was used as control.

§530 ng/100 ml on day 4 before surgery.

In all other subjects the testosterone concentration at the day of or the day before the operation was used as control. The mean variation between duplicate plasma specimens in this series was 20%. The control values were not statistically different from the mean plasma testosterone concentrations previously shown for the 10 medical students before exercise (Table 1). A marked and highly significant decrease of the plasma testosterone concentrations was found during the first two days following the operations ($p < 0{\cdot}001$). In most cases, but not in all (No. I, III and VI were exceptions) a decrease was still notable after 5–6 days ($p < 0{\cdot}01$). In some cases (Table 3) no testosterone levels were obtained for patients on days 17–19 and/or 21–22. In such cases these control values were excluded in the statistical evaluation of the available data for those days. From 9 days after the operations and until the end of this study, 25–57 days after the operation, no difference from the control values were noted for the plasma testosterone concentrations.

The cross-sectional study of plasma LH and FSH concentrations showed no significant changes after the operations except for a decrease of plasma FSH on day 2 (Tables 4 and 5). Individual and mean plasma LH values were sometimes below the lower limit (0·6 ng/ml) of serum LH considered normal for men. Likewise, the statistically significant decrease of FSH on day 2 was not below the lower limit (0·6 ng/ml) of serum FSH usually considered normal. A small apparent decrease in the LH level seemed to occur on day 1 in some individual cases,

Table 4. Plasma LH concentrations of male patients after a major surgical operation

		Control*	Days after operation 1	2	5–6	9–11	13–14	17–19	21–22	25–57
Subject	I	0·5	0·8	0·9	0·6	0·7	0·8	1·0	0·9	
	II	1·0†	0·4	0·3	0·4	0·4	1·0	1·7	1·1	1·0
	III	0·8	0·8	0·6	1·0	0·7	0·7		1·0	0·8
	IV	1·1	0·4	0·7	1·0	1·7	1·1			1·3
	V	0·5	0·5	0·8	0·7	0·6	0·7	0·7	0·9	
	VI	0·6	0·3	0·7	1·0	1·0	0·9			0·8
	VII	1·35‡	1·2	0·9	1·6	1·0	1·3		1·7	1·6
	VIII	1·5	0·7	0·7	0·7	1·2	1·4	0·9	0·8	
Mean		0·92	0·64	0·70	0·88	0·91	0·99	1·08	1·07	0·91
S.D.		0·38	0·30	0·19	0·37	0·41	0·26	0·43	0·33	0·41
t test			N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.	N.S.

*The concentration at the day of or before the operation if not otherwise stated.
†Value 56 days after the operation.
‡Mean of values 5 days before and on the day of the operation.

Table 5. Plasma FSH concentrations of male patients after a major surgical operation

		Control*	Days after operation 1	2	5–6	9–11	13–14	17–19	21–22	25–57
Subject	I	1·3	1·1	1·0	1·3	1·3	1·4	1·6	2·2	
	II	1·5†	0·8	0·7	0·5	0·6	1·0	1·0	1·2	1·5
	III	1·3	1·6	1·5	1·5	1·3	1·5		2·3	2·9
	IV	2·0	1·4	0·8	1·3	2·0	1·6			1·8
	V	1·3	1·3	1·3	1·5	1·7	2·0	1·4	2·0	
	VI	2·2	0·6	0·9	1·5	2·2	1·9			2·0
	VII	2·45‡	1·5	1·3	1·8	1·7	1·6		1·6	2·7
	VIII	1·9	2·0	1·5	1·2	0·9	1·6	1·8	2·2	
Mean		1·74	1·29	1·13	1·33	1·46	1·58	1·45	1·92	2·18
S.D.		0·45	0·45	0·32	0·38	0·54	0·31	0·34	0·43	0·60
P value			$< 0·1$	$< 0·01$	$< 0·1$	N.S.	N.S.	N.S.	N.S.	N.S.

*The concentration at the day of or the day before the operation if not otherwise stated.
†Value 56 days after the operation.
‡Mean of values 5 days before and on the day of the operation.

e.g. patients IV and VI. Individual cases showed decreased FSH levels on day 1(V, VI), on day 2 (I, IV, VII), on day 6 (II) and on day 10 (VIII).

DISCUSSION

The results obtained in this study demonstrate a pronounced decrease of the plasma testosterone concentrations, determined in blood samples taken in the morning, after major surgical operations in the human male with nadir on days 1 and 2 (127 ± 31 and 136 ± 26 ng/100 ml, respectively). The change seems to be more pronounced than previously observed[3, 4], the decreased levels being 10–20% of the control levels. The previously reported postoperative rise[1, 2] was not observed within an observation period of 4–8 weeks [cf. also 5].

Plasma LH concentrations did not change significantly when measured in the same blood samples. The FSH concentrations decreased significantly in the cross-sectional study on day 2 after the operation. This study seemed to obscure the individual variations which showed a decrease of the FSH levels on any day between day 2 and 10. The postoperative decrease of the FSH levels was moderate and not below the lower limit for the normal male range. Although the postoperative change of plasma LH levels was not significant, individual postoperative LH values were observed below the lower limit regarded as normal for LH. It cannot be excluded, however, that this was caused by the use of plasma instead of serum. An isolated LH value may also be of limited value in view of the demonstration of intermittent secretion in men[22]. It is not known whether the same is true for FSH. It is therefore concluded that plasma LH and FSH did not decrease during the postoperative course concomitant with the decrease of the plasma testosterone concentration. In view of the rapid turnover of circulating testosterone (the turnover time is estimated to be about 5 min in adult men [23, 24] giving a lag time, "inertia", of 10 min between a secretory "peak" and a corresponding "peak" in the peripheral circulation) and of the rapid effect of LH and FSH in stimulating the testicular testosterone secretion (within minutes)[25, 26], it can be concluded that the decrease observed in plasma testosterone concentrations cannot be caused by a decrease in the gonadotropic stimulation from the pituitary.

The moderate decrease of plasma FSH observed on day 2 (or even later) may then be secondary to the decrease in plasma testosterone. The mechanism causing the decreased testosterone level may be an effect directly on testicular secretion, independent of the pituitary, or of a decreased specific protein binding. The physiological significance would in either case be entirely different, decreased production leading to a deficiency in this anabolic hormone, decreased binding leading to a release of bound testosterone, an "autoinjection" of testosterone, with subsequent metabolization. Some experimental data in male rats seem to indicate that testosterone administration may decrease plasma levels of LH but not of FSH two days after administration[27]. Testosterone given to castrated male rats caused elevations in pituitary FSH concentration[28, 29]. It is not known whether this effect was caused by increased FSH synthesis or decreased release. Conversely a decreased production of testosterone is expected to give rise to increased FSH and subsequently also increased LH secretion from the pituitary analogous with the effect of hemicastration[30]. There was no indication in the present series of increased plasma FSH or LH levels. This was contrary to Monden *et al.*[5] who observed increased LH levels 6 days after pulmonary lobectomy in a series of 13 patients. They also observed smaller decrease in the plasma testosterone concentrations 1, 2 and 3 weeks after pulmectomy in 42 patients. The decrease of plasma FSH levels observed in our material and of plasma LH levels observed by Monden *et al.* therefore lasted a shorter time than the duration of the decrease in the testosterone concentrations. In occasional patients Carstensen *et al.*[2, 3] found increased plasma LH levels several days after partial gastrectomy, but not in others. The difference between our results and those of Monden *et al.* may be explained by the different type of surgical trauma, pulmectomy probably being more severe and long lasting.

Contrary to Monden *et al.*[5] we observed that the decrease of circulating testosterone levels was already maximal one day after operation. Work is in

Table 6. Analysis of the case histories in connection with the surgery series

Subject	Duration of surgery (h)	Blood loss (ml)	Blood transfusion (ml)	Dextran infusion (ml)				Infusion of various physiological solutions (ml)			
				Day − 1	Day 0	Day 1	Day 2	Day − 1	Day 0	Day 1	Day 2
I	1¾	400	0	0	300	0	0	0	2000	0	0
II	1¼	100	0	0	500	0	0	0	1000	0	0
III	1	—	1000*	0	500	0	0	0	2000	1600	2000
IV	1¾	400	0	0	0	0	0	0	2000	2000	2000
V	2	1800	1000	0	500	0	0	0	2000	2500	2700
VI	1½	100	1000†	0	500	0	0	0	2000	2000	2000
VII	¾	100	1000‡	500	500	0	0	2000‡	2000	1000	0
VIII	2	650	1000	0	0	0	0	0	2000	1600	1100

*Days 4 and 5 before surgery.
†Day 1 and 2.
‡Day 13 before surgery.

Subject	Body temperature			Anxiety, etc..			Haematocrit			Base excess		
	Day 0	Day 1	Day 2	Day 0	Day 1	Day 2	Day 0 or − 1	Day 1	Day 2	Day 0	Day 1	Day 2
I	37·5	38·0	37·5	No	No	No	46	40	37	—	—	—
II	37·2	37·3	37·2	No	No	No	—	30	25			
III	36·6	37·5	37·5	No	No	No	28*	32	30†	—	−3·5	—
IV	36·3	36·1	36·9	No	Yes	Yes	48	43	34	—	—	—
V	36·5	38·5	38·0	No	No	Yes	42	41	42	—	—	±0‡
VI	36·6	37·8	37·2	No	Pain	No	38	29	29	—	−3·1	+1·0
VII	37·0	37·2	37·6	No	No	No	35	29	28	±0	—	—
VIII	36·5	38·5	37·6	No	No	No	41	39	42	−5·1	−5·1	+3·0

*Day 4 before surgery.
†Day 3 before surgery.
‡Day 6 before surgery.

progress in this laboratory in order to elucidate the mechanism of the post-operative decrease.

Physical exercise did not influence the plasma testosterone concentration in young males in spite of its profound effect on the metabolism, e.g. acidosis[31], sympathetic and adrenal medullary activation, and the role of testosterone demonstrated in exercise-induced glycogen supercompensation[32].

It is premature to draw conclusions as to which factor or factors in connection with major surgical operations are responsible for the decrease in plasma testosterone levels before more is known about the mechanism by which this is brought about. In treating the effect of surgical trauma on the activation of adrenocortical hormone secretion, the polyvalent nature of the surgical stimulus was emphasized by Francis D. Moore[33]. We have attempted to analyse some of these factors in connection with eight subjects studied, e.g. blood loss, dextran and blood infusion before, during and after the operation, duration of the operation, premedication, anaesthesia, anxiety, water, electrolyte and acid-base balance (Table 6). In fact the most pronounced decrease of plasma testosterone concentration was observed in Subject II who had a very small blood loss, received no blood transfusion and was given less dextran than some of the others and who was anaesthetized by spinal anaesthesia and had an operation of moderate duration. However because of the extensive leg fractures received in a traffic accident Subject II is expected to have suffered a great deal of mental and physical trauma. Also Werder *et al.*[34] observed that general anaesthesia (endotracheal halothane plus nitrous oxide) produced increased plasma cortisol levels in connection with the intubation and excitation phase followed by decreased levels. Only after more than 4–5 h a second increase occurred. However in no case did the anaesthesia in our series last longer than 2 h. Pentobarbital has been shown to inhibit testosterone secretion and biosynthesis in dogs[35]. However barbiturates were not used in subjects I and II, yet their testosterone levels decreased notably. In the other subjects (III–VIII) a barbiturate was given only as an induction to endotracheal narcosis. It is therefore concluded that the anaesthesia is of negligible importance and that the physical trauma of surgery is the most important factor causing the decreased plasma testosterone concentration after surgical operations in human males. One observation of ours may further strengthen this point of view. It was observed that after a 6 day history of gastric ulcer with haematemesis, compensated by blood transfusions and dextran infusions but without surgery or anaesthesia, perforation occurring 6 h before operation was accompanied by strongly decreased plasma testosterone concentration, amounting to 182 ng/100 ml (Subject III).

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