THE INFLUENCE OF CERTAIN STEROID HORMONES ON THE THYROID UPTAKE OF IODINE AND ON THE RENAL EXCRETION OF IODINE AND OTHER ELECTROLYTES

A Thesis

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Master of Science

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by

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PART I

THE INFLUENCE OF CERTAIN STEROID HORMONES ON THE THYROID UPTAKE OF IODINE

INTRODUCTION

In recent years there has been a renewed interest in the thyroid-adrenal interrelationship, especially in the influence of steroid hormones on the thyroid function. The findings in the older literature (1 - 12), usually reporting clinical and experimental evidence for an inhibitory action of adrenal cortical hormones on the thyroid gland, have to be reassessed with newer methods and the now available more purified hormones.

It has been generally established that ACTH and cortisone have a depressing action on the thyroid function as measured by the thyroid uptake of radioactive iodine in man (13 - 18) and in the rat (19 - 25). There are a few reports not in accord with these observations (26, 27). There has been relatively little reported on the effect of other steroid hormones on the thyroid function especially in man and the reported results are conflicting. DOCA has been reported to have no effect in the rat (28) and to increase the thyroid iodine concentration in both adrenalectomized rats (29) and normal rats (30) and in guinea pigs (9). On the other hand DOCA has been reported to have a protective action against excessive thyroxine administration (31).

Inconsistent results have been reported concerning the influence of oestrogenic hormones on the thyroid function; the older literature has been reviewed by Farbmann (32). Evidence has been presented for an ovarian-thyroid antagonism (33), but both ovariectomy and oestrogen administration failed to influence the ability of the

thyroid gland to take up I^{131} (34). Corpus luteum extract has been believed to improve Graves' disease (35). However Money et al. (19) report an increased collection of iodine by the rat thyroid gland following treatment with oestrone, progesterone and testosterone and decreased collection after pregnenolone. Other steroids investigated include the cardiac glucosides which have been shown to have a depressant action similar to that of adrenal cortical hormones (31, 36).

The purpose of this communication is to present data on the inhibitory action of cortisone and DOCA on some aspects of the thyroid function in the human together with observations on the influence of oestradiol, progesterone, and testosterone on the ability of the thyroid gland to take up iodine.

SUBJECTS AND METHODS

The majority of the subjects of these experiments were patients on the psychopathic ward of the Winnipeg General Hospital. As far as could be ascertained they had no organic diseases and had undergone no shock therapy or surgery within at least a year prior to the study and none of the patients had been taking iodine in amounts other then encountered in ordinary diets. A few of the patients were from other services but had no thyroid, adrenal, renal or circulatory disorders and had been on normal diets and were receiving no iodine containing medication. All subjects are listed in table I with details regarding their diagnoses, age, sex, etc.

TABLE I

CLINICAL DETAILS

Subject	Sex	Age	Treatment	Diagnosis
T.K.	M	18	DOCA	Tuberculosis of ankle; Arthrodesis
W.O'C	M	38	DOCA	Psychosis with mental deficiency
D.C.	M	22	DOCA	Schizophrenia affective psychosis
G.S.	M	50	DOCA	Mental deficiency with psychotic episodes
R.A.	M	27	DOCA	Schizophrenia, paranoid
H.B.	F	41	DOCA	Neurotic depressive reaction
W.P.	M	17	DOCA	Primary behaviour disorder
E.L.	F	22	DOCA	Psychosis, mental deficiency
A.S.	F	21	DOCA	Schizophrenia affective psychosis
H.M.	F	21	DOCA	Schizophrenia, paranoid
T.T.	M	31	DOCA	Chronic Alcoholism*
R.R.	M	35	DOCA	Parkinsonism, postencephalitic
R.F.	F	51	Cortisone	Rheumatoid arthritis
J.O'L.	M	32	Cortisone	Schizophrenia, paranoid
L.R.	M	39	Cortisone	Manic depressive; depressed
M.C.	M	31	Cortisone	Manic depressive; manic
P.E.	M	39	Cortisone	Simple Schizophrenia
D.E.	F	23	Cortisone	Psychoneurosis, anxiety state
J.S.	M	17	Oestradiol	Schizophrenia, catatonic
A.L.	M	43	Oestradiol	Schizophrenia, paranoid
W.M.	M	27	Oestradiol	Chronic alcoholism*
C.M.	M	23	Progesterone	Incipient Schizophrenia
A.B.	M	49	Progesterone	Immature personality, emotional instability
J.Y.	M	20	Progesterone	Psychoneurosis, anxiety state
S.M.	M	26	Testosterone	Simple Schizophrenia
J.M.	M	19	Testosterone	Schizophrenia, catatonic
C.S.	M	31	Testosterone	Schizophrenia, paranoid
V.R.	F	32	Testosterone	Simple Schizophrenia

* Off alcohol and on treatment for several weeks

The same procedures were carried out twice on all patients - once before and once after treatment with the various steroids, each patient thus acted as his own control. The experiments were carried out at the same time of the day each time under as similar conditions as possible.

After a 14 hour fast the subjects were given 75 - 100 microcuries radioiodine orally. Approximately two hours later the bladder was emptied, the exact time noted and almost simultaneously a blood sample taken and counts made over the thyroid area to measure the thyroid uptake of iodine. Two hours later these procedures were repeated and the exact time again noted, the urine passed during the exactly timed period was collected and saved.

The patients carried out their usual ward activities but remained fasting during all this period and were usually kept well hydrated, 200 ml. of water being given to drink approximately every hour from the time of administration of the radioiodine.

26 hours after the ingestion of the radioiodine the thyroid uptake was again determined and a third blood sample taken. The thyroid uptake was again determined 24 hours later - 50 hours after the dose.

Following the 50 hour count treatment was commenced with the various steroids. After three full days of steroid treatment the procedures described above were all repeated, the administration of the hormone under investigation being continued during this time.

At the time of the second dose of radioiodine (110 - 130 microcuries) there were of course appreciable amounts of radioactivity still in the thyroid. This amount was determined just prior to the administration of the second dose of the isotope and deducted from the ensuing thyroid counts, appropriate corrections for its isotope decay being made each day.

The amount of radioactivity present in the thyroid gland was measured by means of a shielded collimated scintillometer (Scintillometer Model 939. Halross Instruments Corp. Winnipeg, Canada), readings being taken 6 inches above the thyroid isthmus and compared with similar counts taken 6 inches above a 25 ml. glass bottle containing an aliquot of the dose of I^{131} given to the patient, in this way expressing the thyroid I^{131} as a percentage of the given dose. Thyroid counts were corrected by subtracting a background count taken 6 inches over the mid thigh and the standard counts by subtracting the background counts of the experimental area.

The blood samples were collected in heparin and the plasma immediately separated. The radioactive iodine concentrations in plasma and urine were measured by the procedures described in a previous communication from this laboratory (37). Early in the experiment it was found that the estimation of the radioactive iodine in the urine by means of a calibrated liquid counter of the Veall type (38) gave identical results as the more time consuming precipitation method employed previously. Later on only the liquid counter was used.

Protein bound plasma iodine and urinary stable iodine (I^{127}) were estimated by Barker's method (39).

From the amounts of radioiodine in plasma determined at two known times and from the amount of I^{131} taken up by the thyroid gland and excreted in the urine during this known time interval one is able to calculate the rate of clearance of plasma of I^{131} by the thyroid (40, 41). The thyroid clearance was calculated from the formula $\frac{\text{thyroid uptake per minute}}{P}$, where P represents the logarithmic mean plasma concentration (42, 43): $\frac{P_1 - P_2}{\log_e P_1 - \log_e P_2}$.

The stable iodine (I^{127}) concentration of the plasma during the clearance period was calculated using the method of Stanley (44) which by assuming complete mixing of the two isotopes it follows that the ratio $\frac{I^{131}\text{ concentration}}{I^{127}\text{ concentration}}$ in urine and plasma is the same and thus knowing the urinary I^{131} and I^{127} concentrations and the plasma I^{131} concentration, the plasma I^{127} concentration is readily calculated. Similarly a calculation of the I^{127} uptake by the thyroid gland can be made.

Total plasma protein determinations were made by the method of Phillips et al. (45).

The statistical analyses were based on the method "Significance of a mean of a small sample", described by Fisher (46). The use of this method is justified because the same patients were tested before and after the administration of a hormone. A statistical analysis of

the small groups treated with oestradiol, progesterone and testosterone was not attempted.

The influence of the steroids desoxycorticosterone, cortisone, oestradiol, progesterone and testosterone was investigated, the administration of these compounds was as follows:

Desoxycorticosterone acetate (Percorten Ciba): 10 mgm. IM daily in two divided doses 12 hours apart for a total of 6 days.

Cortisone acetate (Cortone Merck, for oral use):
Day 1: 250 mgm. in three divided doses, 8 hours apart;
Day 2 and 3: 150 mgm. in three divided doses, 8 hours apart;
Day 4: 200 mgm. in three divided doses, 8 hours apart;
Day 5: 150 mgm. in three divided doses, 8 hours apart;
Day 6: 50 mgm. at 6 AM.

Testosterone propionate (Perandren Ciba): 25 mgm. IM daily in two divided doses, 12 hours apart for a total of 6 days.

Oestradiol benzoate (Ben-ovocyclin Ciba): 12 mgm. IM daily in two divided doses, 12 hours apart for a total of 6 days.

Progesterone (Lutocyclin Ciba): 25 mgm. IM daily in two divided doses, 12 hours apart for a total of 6 days.

RESULTS

EFFECT OF DOCA ON THYROID FUNCTION

In figure 1 the percentage of the dose of radio-active iodine present in the thyroid gland at various times are compared in 12 subjects before and after treatment with DOCA. In all patients the percent uptake was lower after the treatment at each time with the exception of two patients (T.K. and D.C.) whose 26-hour and 50-hour counts, respectively, were slightly increased after 5 days on DOCA.

In Table II are shown the values of the thyroid accumulation rate of stable and radio-active iodine, and the thyroid clearance of radio-iodine observed in the same 12 patients before and after administration of DOCA. Also shown in this table is the calculated plasma I^{127} level, the protein bound iodine and the total plasma proteins.

As may be seen in Table II there was a marked depression of the thyroid function as measured by iodine uptake and I^{131} clearance after three days treatment with 10 mgm. of DOCA per day. Although the plasma level of I^{127} tended to rise, the uptake of stable iodine by the thyroid gland was depressed. Both protein bound iodine and total plasma proteins were lower after the DOCA treatment, the decrease in plasma proteins being highly significant.

Some patients showed a slight increase of the body weight under the treatment with DOCA.

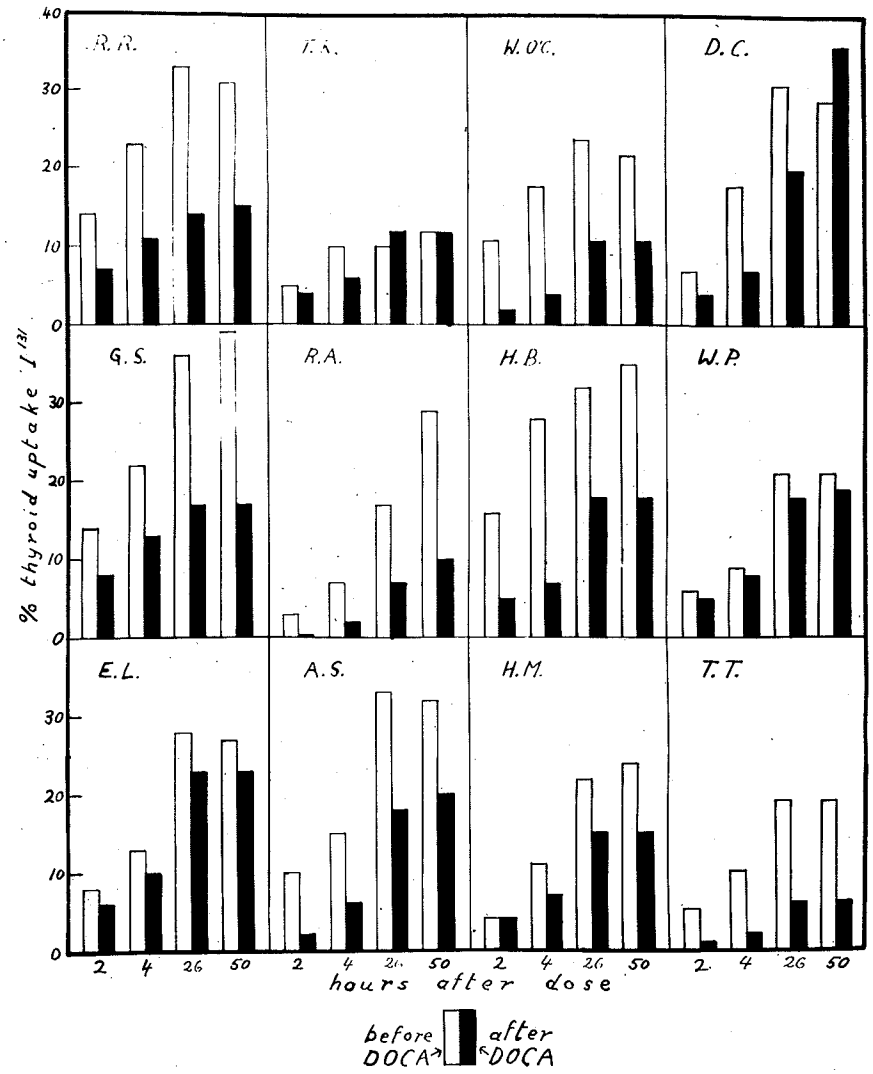

Fig. 1. The thyroid uptakes in 12 subjects before and after treatment with DOCA for three days.

TABLE II

THYROID FUNCTION IN TWELVE PATIENTS BEFORE AND AFTER TREATMENT WITH DOCA

Subject	Thyroid uptake I^{131} % / hour		Thyroid uptake I^{127} µgm./hour		Thyroid clearance I^{131} ml./min.		Mean plasma I^{127} µgm. %		Protein bound Iodine µgm. %		Plasma proteins gm. %	
	before	after	before	after	before	after	before	after	before	after	before	after
T.K.	1.71	0.89	1.81	0.49	10.6	2.0	0.28	0.30	4.9			
W.O'C.	3.60	0.94	1.11	0.60	21.8	6.0	0.09	0.17	3.5			
D.C.	5.54	2.26	3.32	2.51	30.5	11.5	0.18	0.36	2.3			
G.S.	4.35	2.24	1.47	0.63	23.4	10.5	0.10	0.10	6.7			
R.A.	1.74	0.71	2.68	1.78	7.1	3.4	0.63	0.87	4.2			
H.B.	5.66	1.23	2.66	1.19	24.2	6.5	0.18	0.34	4.8	3.7	6.4	5.7
W.P.	1.80	1.60	0.86	0.64	9.5	8.9	0.15	0.12	5.3	4.0	7.2	6.3
E.L.	2.04	2.16			14.9	16.5			8.8	5.7	6.3	5.8
A.S.	2.49	2.11	2.43	2.33	16.1	12.3	0.25	0.31	5.5	6.0	6.9	6.7
H.M.	4.05	1.34	4.05	1.34	17.9	6.8	0.36	0.21	8.3	7.5	6.8	6.2
T.T.	2.27	0.37	2.27	0.37	11.5	2.7	0.25	0.32	7.0	7.0	6.6	5.5
R.R.	3.46	2.10			20.6	2.6						
Mean ± s.e.	3.23 ±0.40	1.49 ±0.19	2.27 ±0.31	1.18 ±0.25	17.4 ±2.0	7.5 ±1.3	0.25 ±0.03	0.31 ±0.07	6.6 ±0.7	5.5 ±0.7	6.7 ±0.1	6.0 ±0.2
Mean difference ±s.e.	-1.73±0.40		-1.08 ±0.25		-9.9 ±2.03		+0.06±0.04		-1.1 ±0.55		-0.7 ±0.13	
p value	< 0.01		< 0.01		< 0.01		> 0.05		> 0.05		< 0.01	

Further observations on the action of DOCA on the renal excretion of iodine in these subjects are reported in part II where it is shown that DOCA did not increase the renal clearance of iodine and hence the lower uptake of iodine by the thyroid was not a result of an increased excretion by the kidney.

EFFECT OF CORTISONE ON THYROID FUNCTION

The action of this steroid was observed on 6 subjects. The thyroid uptakes 2, 4, 26 and 50 hours after the administration of I^{131} before and after cortisone are shown in figure 2, the results obtained being similar to these noted following the treatment with DOCA: a depression of the percent of dose taken up by the thyroid gland at these time intervals. In two subjects the two hour uptakes were only slightly lower after cortisone but the 4, 26 and 50 hour uptakes were markedly depressed.

In Table III are shown various values of the six patients before and after three days treatment with cortisone.

Cortisone depressed the thyroid clearance rate of radio-active iodine and the accumulation rates of both the radio-active and the stable iodine, the depression of the clearance rate and the accumulation of I^{131} being highly significant. Unlike the result with DOCA no alteration in the plasma level of I^{127} and in the plasma proteins or in protein bound iodine levels were noted after cortisone, neither did the body weight change.

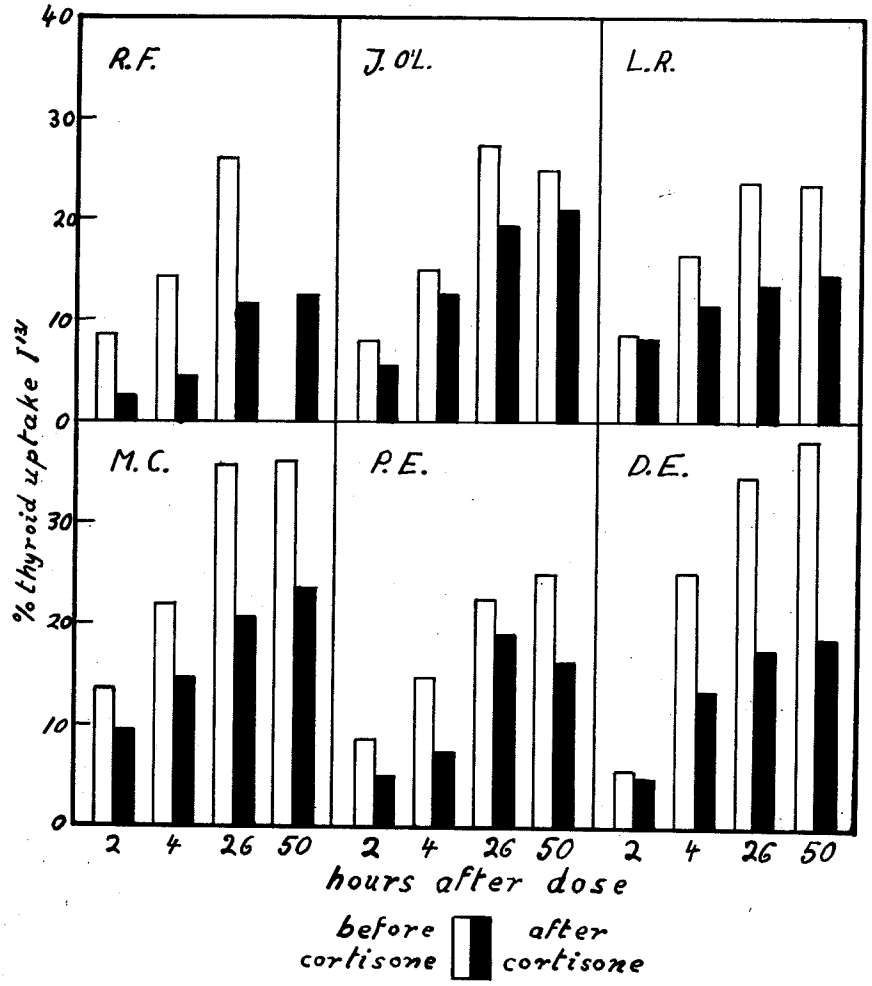

Fig. 2. The thyroid uptakes in 6 subjects before and after treatment with cortisone for three days.

TABLE III

THYROID FUNCTION IN SIX PATIENTS BEFORE AND AFTER TREATMENT WITH CORTISONE

Subject	Thyroid uptake I^{131} % / hour		Thyroid uptake I^{127} µgm./hour		Thyroid clearance I^{131} ml./min.		Mean plasma I^{127} µgm. %		Protein bound Iodine µgm. %		Plasma proteins gm. %	
	before	after	before	after	before	after	before	after	before	after	before	after
R.F.	2.7	1.0	1.6	0.3	14.4	8.3	0.18	0.06	3.0	3.5	6.4	6.3
J.O'L.	3.6	2.7	3.8	2.0	24.8	22.6	0.25	0.15	2.3	2.5	6.2	6.7
L.R.	3.8	1.5	1.8	1.5	18.3	11.4	0.17	0.22	3.3	3.3	5.8	6.0
M.C.	4.2	2.3	2.7	1.7	22.1	18.3	0.20	0.16	3.6	3.8	5.7	5.8
P.E.	2.9	1.0	5.0	2.0	17.2	5.2	0.48	0.66	4.2	4.2	6.9	6.7
D.E.	6.2	4.3	1.6	1.6	31.9	26.4	0.09	0.10	4.5	4.5	6.9	7.1
Mean ± s.e.	3.9 ±0.6	2.1 ±0.6	2.8 ±0.6	1.5 ±0.3	21.5 ±2.8	15.4 ±3.4	0.23 ±0.06	0.23 ±0.09	3.5 ±0.4	3.6 ±0.4	6.3 ±0.2	6.4 ±0.2
Mean difference ± s.e.	-1.8 ±0.22		-1.2 ±0.44		-6.1 ±1.37		0		0		+0.2 ±0.1	
p value	<0.01		<0.05 >0.02		<0.01						>0.05	

EFFECT OF OESTRADIOL, PROGESTERONE AND TESTOSTERONE ON THE THYROID FUNCTION

This group consists of 10 subjects; three were treated with oestradiol, three with progesterone and four with testosterone. In figure 3 are shown the thyroid uptakes of I^{131} 2, 4, 26 and 50 hours after the ingestion of radio-active iodine before and after treatment with the various hormones.

It may be seen that only the administration of progesterone was followed by a depression similar to that after DOCA or cortisone. No apparent changes are induced by the administration of testosterone. The response to oestradiol was inconsistent: depression in two cases, no changes in one.

In Table IV are again shown the accumulation rates of both stable and radio-active iodine, the thyroid clearance rates of radio-active iodine, and the plasma levels of I^{127}, the protein bound iodine and the total plasma proteins.

None of the three subjects treated with oestradiol showed consistent changes in the thyroid function. In J.S. who showed an increased I^{127} uptake and a higher plasma level of I^{127} following oestradiol, an increased iodine intake between the two determinations is suspected to have occured.

The accumulation rates of both isotopes of iodine and the thyroid clearance of radio-active iodine showed a tendency to decrease after progesterone; the changes in the plasma levels are inconsistent.

A few findings are missing in the group treated with testosterone

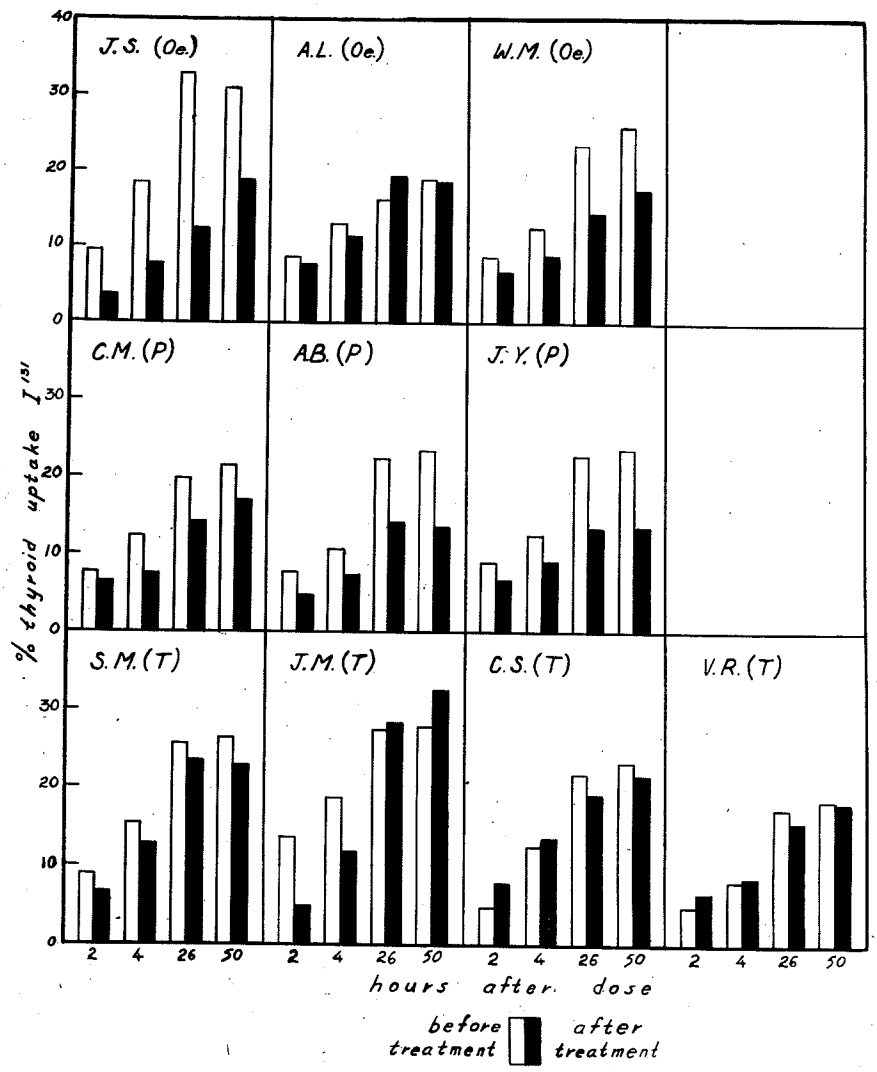

Fig. 3. The thyroid uptakes in 10 subjects before and after treatment with oestradiol (Oe), progesterone (P) or testosterone (T) for three days.

TABLE IV

SUBJECTS TREATED WITH OESTRADIOL (Oe), PROGESTERONE (P), TESTOSTERONE (T)

Subject	Treatment	Thyroid uptake I^{131} % / hour		Thyroid uptake I^{127} mgm./hour		Thyroid clearance I^{131} ml./min.		Mean plasma I^{127} mgm. %		Protein bound Iodine mgm. %		Plasma proteins gm. %	
		before	after	before	after	before	after	before	after	before	after	before	after
J.S.	Oe	4.0	2.1	1.6	6.6	29.8	17.7	0.09	0.63	4.2	3.9	6.3	6.5
A.L.	Oe	2.3	1.7	1.2	0.7	9.4	9.7	0.21	0.13	4.1	3.0	6.2	6.0
W.M.	Oe	2.1	1.6	2.5	2.3	10.6	13.0	0.38	0.29	3.0	4.2	5.8	5.8
C.M.	P	2.2	0.6	1.8	0.7	7.1	3.2	0.42	0.34	4.0	3.5	6.0	6.0
A.B.	P	1.5	1.0	1.8	1.2	8.0	7.0	0.39	0.33	3.8	3.3	6.7	6.7
J.Y.	P	2.0	1.2	1.5	1.1	10.5	4.4	0.27	0.41	5.0	4.2	7.3	6.9
S.M.	T	2.9	2.9	-	-	19.0	16.6	-	-	4.3	4.4	6.5	6.4
J.M.	T	2.6	3.1	-	-	20.6	19.6	-	-	2.7	4.3	6.7	6.4
C.S.	T	4.5	2.8	3.2	2.6	37.6	15.6	0.16	0.28	2.7	2.6	6.1	6.0
V.R.	T	1.6	1.3	0.4	1.1	5.6	4.2	0.10	0.45	6.6	7.4	6.5	6.5

because of incomplete urine collections. The thyroid clearance of I^{131} showed a slight tendency to decrease on the four patients, but only in one patient (C.S.) the uptake of iodine during the clearance period was depressed.

No consistent changes in the protein bound iodine were observed after oestradiol, progesterone and testosterone and no changes in the total plasma proteins occured. The body weight was not influenced by these hormones.

DISCUSSION

Although the majority of the subjects of this study were psychotic individuals, mainly schizophrenics, there is no reason to suppose that their thyroid glands reacted to the steroids differently than those of mentally normal individuals. This problem is discussed in Part III.

The rate of uptake of both stable and radio-active iodine and also the rate of clearance of I^{131} of plasma by the thyroid were markedly depressed by desoxycorticosterone as well as by cortisone. Thus the two adrenal cortical hormones have in common a depressant action on the thyroid gland, though it appears on a weight basis that DOCA is more potent than cortisone in this respect.

No definite conclusion can be drawn from the observations on the subjects treated with oestradiol. The calculated mean plasma level of I^{127} of J.S. was so much higher when it was determined the second time, that an uncontrolled increased dietary intake (e.g. cough

medicine) immediately before the second determination is suspected. A significant alteration of the thyroid function apparently did not occur.

The group of patients treated with progesterone is too small to be analyzed statistically. The findings suggest however, that a depression of the thyroid function took place, comparable to that of DOCA or cortisone. In view of the close similarity of the chemical structures of DOCA and progesterone, a similar action of these two hormones is not unexpected.

Testosterone does not seem to alter the thyroid function. One of the four patients however (C.S.), shows some evidence of a depression. Again no definite conclusions based on this small group are justified.

The depressed accumulation of radio-active iodine induced by DOCA need not be an indication of a depression of this aspect of the thyroid function for it might be a result of the dilution of the I^{131} by retained stable I^{127} manifest by somewhat increased plasma iodine levels. However the simultaneous depression of the rate of thyroid uptake of stable iodine together with the depressed thyroid clearance rate of I^{131} would indicate a real depression of the ability of the thyroid gland to concentrate iodine from the plasma. Further similar findings were observed with cortisone and progesterone where there was evidently no elevation of plasma iodine.

It is noteworthy that a patient with a depressed thyroid function as evidenced by a low uptake of radio-active and stable iodine, a low iodine clearance and a low protein bound iodine showed a further

depression after the administration of DOCA.

During the second examination possible changes in the amount of radio-active iodine left over from the first tracer dose are not accounted for. In addition to the isotope decay this radioactivity decreases continuously due to the secretion of thyroxine labelled with I^{131} given in the first dose. The difference between the effective half life and the physical half life during the first three days after the tracer dose is small (47). The rate of secretion might be affected by the hormones. In order to reduce the error caused by uncontrolled changes in the I^{131} content of the thyroid gland, the second dose was always considerably larger than the first one.

No alterations in the plasma levels of protein bound iodine were noted following cortisone administration contrary to other reports (14, 15), but in the present experiments the measurements were made after only three days treatment. The possible slight fall in protein bound iodine following DOCA administration may well have been the result of an increase in plasma water which occurs after administration of this substance (48, 49). The slight but consistent drop in plasma protein concentration in all DOCA patients suggests that this took place. Following the administration of cortisone, oestradiol, progesterone and testosterone as well as no change in protein bound iodine levels there was no alteration in the concentration of the plasma proteins.

The mechanism of the antithyroid action of the adrenal cortical hormones is controversial. It appears established that the effect of cortisone is not mediated by means of an inhibition of pituitary thyrotrophin (22, 23, 50) but possibly by means of an inhibition of the thyrotrophin action at the target organ level (51). DOCA can be presumed to act in a similar manner. Unpublished work from this laboratory (52) on the action of DOCA on the thyroid function in the rat indicates that the inhibition of the thyroid gland is not mediated via an inhibition of thyrotrophin in the pituitary.

A decreased uptake of iodine by the thyroid gland could possibly be merely a reflection of an increased renal excretion of iodine, but if so, this should not affect the thyroid clearance rate of iodine, which in fact was also depressed. An increased renal clearance of iodine paralleling the decreased thyroid uptake rate has been reported after several days treatment with cortisone. (17, 53). In the present experiment no consistent alterations in renal clearance of iodine were noted after three days treatment with DOCA or cortisone. The influence of this treatment on some aspects of the kidney function and on the plasma iodide concentration is discussed in Part II.

SUMMARY AND CONCLUSIONS

The thyroid function has been investigated in 28 subjects before and after receiving 10 mgm. desoxycorticosteroneacetate, or 150 - 250 mgm. cortisone, or 12 mgm. oestradiol, or 25 mgm. progesterone, or 25 mgm. testosterone, respectively, daily for three days. The thyroid

gland is markedly depressed after administration of DOCA and cortisone as evidenced by a low uptake of both radio-active and stable iodine, and by a low thyroid clearance of I^{131}. There appears to be a similar depression after progesterone. Testosterone in the given dosage does not seem to influence the thyroid gland, whereas the administration of oestradiol was followed by inconsistent changes.

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PART II

THE INFLUENCE OF DESOXYCORTICOSTERONE, CORTISONE AND PROGESTERONE ON THE RENAL EXCRETION OF IODINE AND OTHER ELECTROLYTES

INTRODUCTION

The effect of DOCA and Cortisone on renal function in general and on the excretion of electrolytes, especially sodium, potassium and chlorine, has been studied intensively in man and animals under various experimental conditions (1-30). Although it is generally assumed that the organism cannot distinguish sharply between the various halide ions (31-35), little data has actually been reported on the effect of these hormones on the renal excretion of iodine.

In Part I data is presented on the influence of various steroid hormones on the thyroid uptake of iodine. During these experiments miscellaneous observations on the renal excretion of iodide and chloride, potassium and sodium were made which form the basis for the present communication.

SUBJECTS AND METHODS

Details concerning the subjects on whom this study was carried out and a description of the experiment are given in Part I. In addition, the following experimental procedures were used for the investigation of the kidney function.

The renal clearance of I^{131} was calculated from the usual formula $\frac{uv}{P}$, where P is the logarithmic mean concentration of the I^{131} concentration determined in the two blood samples (36-37).

Endogenous creatinine clearance was determined as a measure of the glomerular filtration rate, having been shown to be a fair approximation of inulin clearance (38,39). The values for renal clearance of creatinine and iodide were standardized to a body surface of $1.73m^2$, this estimation being based on the weight taken at the time of the first clearance period, any weight change due to the steroid treatment being neglected.

The stable iodine (I^{127}) concentration of the plasma was calculated using the method of Stanley (40).

The plasma chlorides were estimated according to the method of Schales and Schales (41), urine chlorides by the method of Volhard - Arnold (42). Sodium and potassium in plasma and urine were determined by flame-photometry.

The amount of radio-active iodine left over from the first dose which is present in the blood or urine, being very small at the time of the second examination, was negligible and was not taken into account.

The dosage of the various hormones was the same as described in Part I.

RESULTS

The glomerular filtration rates, measured as endogenous creatinine clearance, was very variable before and after the treatment with the hormones. As can be seen in Table I, the means do not differ significantly. After DOCA a slight increase and after cortisone a slight decrease appears to have occurred. The findings after progesterone were not consistent.

No correlation between the glomerular filtration rate and the renal clearance of iodine, before and after the treatment, could be found. The individual changes in glomerular filtration rate and renal clearance of iodide frequently paralleled each other in the subjects treated with cortisone, but not following DOCA or progesterone.

The mean plasma level of radio-active iodine during the clearance period, the plasma level of I^{131} 26 hours after the tracer dose and the calculated mean plasma concentration of stable iodine during the clearance period are presented in Table II. After DOCA the average I^{131} concentration was slightly lower during the second clearance period, whereas the I^{127} concentration was slightly higher; but these changes were not statistically significant. The 26-hour concentration of I^{131} was practically unchanged. After cortisone,

TABLE I

GLOMERULAR FILTRATION RATE AND RENAL CLEARANCE OF I^{131}
BEFORE AND AFTER HORMONAL TREATMENT

Subject	Treatment	Glomerular Filtration Rate ml/min /1.73m^2		Renal Clearance of I^{131} ml/min /1.73m^2	
		before	after	before	after
T.K.	DOCA	141	162	36.5	27.4
W.O'C.	DOCA	117	216	40.6	57.0
D.C.	DOCA	108	153	39.8	37.3
G.S.	DOCA	163	139	36.9	37.0
R.A.	DOCA	132	148	22.9	26.2
H.B.	DOCA	111	101	21.7	13.0
W.P.	DOCA	172	117	23.6	33.0
E.L.	DOCA	144	174	28.9	7.5
A.S.	DOCA	99	107	21.6	20.7
H.M.	DOCA	117	94	19.3	25.5
T.T.	DOCA	129	143	24.6	31.6
Mean ±S.E.		130 ±6.9	141 ±10.8	28.8 ±2.6	28.7 ±4.2
Mean difference ±S.E.		+11 ±12.3		-0.02 ±3.14	
P value		>0.05		>0.05	
R.F.	Cortisone	82	62	38.8	72.5
J.O'L.	Cortisone	113		26.2	
L.R.	Cortisone	128	113	29.4	28.5
M.C.	Cortisone	191	41	18.9	11.7
P.E.	Cortisone	111	105	27.7	15.7
D.E.	Cortisone	132	191	31.1	44.8
Mean ±S.E.		126 ±14.8	102 ±25.8	29.2 ±3.1	34.6 ±11.0
Mean difference ±S.E.		-26 ±34		+5.5 ±8.3	
P value		>0.05		>0.05	
C.M.	Progesterone	135	162	21.6	32.8
A.B.	Progesterone	107	122	22.9	32.0
J.Y.	Progesterone	125	82	29.1	16.1

TABLE II

BLOOD LEVELS OF IODINE BEFORE AND AFTER HORMONAL TREATMENT

Subject	Treatment	Mean Plasma I^{131} %/100 ml		26-hour Plasma I^{131} %/100 ml		Plasma I^{127} µgm/100 ml	
		before	after	before	after	before	after
T.K.	DOCA	0.269	-	0.023	-	0.28	0.39
W.O'C.	DOCA	0.275	0.260	0.040	0.065	0.09	0.17
D.C.	DOCA	0.298	0.327	0.042	0.073	0.18	0.36
G.S.	DOCA	0.309	0.354	0.032	0.031	0.10	0.10
R.A.	DOCA	0.410	0.344	0.169	0.075	0.63	0.87
H.B.	DOCA	0.389	0.356	0.042	0.036	0.18	0.34
W.P.	DOCA	0.316	0.298	0.032	0.049	0.15	0.12
E.L.	DOCA	0.228	0.218	0.022	0.074		
A.S.	DOCA	0.258	0.285	0.039	0.098	0.25	0.31
H.M.	DOCA	0.378	0.326	0.052	0.039	0.36	0.21
T.T.	DOCA	0.327	0.226	0.048	0.031	0.25	0.32
R.R.	DOCA	0.288	-	0.035	0.016		
Mean		0.312	0.299	0.052	0.053	0.25	0.32
±S.E.		±0.016	±0.016	±0.013	±0.009	±0.03	±0.07
Mean difference		-0.019		+0.003		+0.06	
±S.E.		±0.015		±0.040		±0.040	
P		>0.05		>0.05		>0.05	
R.F.	Cortisone	0.312	0.205	0.028	0.027	0.16	0.06
J.O'L.	Cortisone	0.240	0.199	0.023	0.019	0.25	0.15
L.R.	Cortisone	0.356	0.219	0.045	0.023	0.17	0.22
M.C.	Cortisone	0.318	0.207	0.044	0.018	0.20	0.16
P.E.	Cortisone	0.280	0.328	0.048	0.038	0.48	0.66
D.E.	Cortisone	0.323	0.272	0.047	0.028	0.09	0.10
Mean		0.305	0.238	0.039	0.026	0.23	0.23
±S.E.		±0.127	±0.163	±0.011	±0.007	±0.06	±0.09
Mean difference		-0.067		-0.014		0	
±S.E.		±0.0273		±0.004			
		<0.05		<0.05			
P		>0.02		>0.02			
C.M.	Progesterone	0.505	0.312	0.072	0.060	0.42	0.34
A.B.	Progesterone	0.322	0.291	0.082	0.019	0.39	0.33
J.Y.	Progesterone	0.359	0.440	0.098	0.154	0.27	0.41

however, the concentration of radio-active iodine was significantly depressed during the clearance period and 26 hours after the dose, whereas the stable iodine remained unchanged. After progesterone the changes were not consistent.

The plasma chloride concentration and the Cl-clearance are shown in Table III. The average values were not significantly influenced by the hormone administration though the clearance rate appeared to increase slightly in all three groups.

The same data on sodium is presented in Table IV. Again no significant changes were found and no correlation between the glomerular filtration rate and the sodium clearance was observed.

As may be seen in Table V, the plasma concentration of potassium decreased after the administration of DOCA and cortisone, the decrease after DOCA being significant. The potassium clearance was slightly decreased after cortisone and tended to increase after progesterone.

In Figure 1 the differences in Cl-clearance, induced by the hormone treatment, are compared with the differences in I-clearance and graphically charted. It may be seen that no correlation between these two values could be found.

In addition to the reported data, various other values were calculated, e.g. the excretion rate and the percentage tubular reabsorption, which showed no significant changes after the treatment.

TABLE III

PLASMA LEVEL OF Cl AND Cl-CLEARANCE BEFORE AND AFTER HORMONAL TREATMENT

Subject	Treatment	Plasma Cl mg%		Cl-Clearance ml/min	
		before	after	before	after
T.K.	DOCA	348	321	1.01	2.00
W.O'C.	DOCA	372	369	2.66	2.64
D.C.	DOCA	395	377	2.26	3.36
G.S.	DOCA	400	375	2.05	2.14
R.A.	DOCA	395	402	0.40	1.64
H.B.	DOCA	369	392	1.06	0.63
W.P.	DOCA	355	360	2.41	7.58
E.L.	DOCA	300	371	1.12	0.74
A.S.	DOCA	362	348	1.96	0.95
H.M.	DOCA	380	447	0.58	1.33
T.T.	DOCA	364	360	2.32	1.83
R.R.	DOCA	376	344		
Mean		373	372	1.62	1.80
±S.E.		±4.8	±0.7	±0.27	±0.26
Mean difference		-1		+0.18	
±S.E.		±7.85		±0.20	
P		>0.05		>0.05	
R.F.	Cortisone	350	382	2.14	3.32
J.O'L.	Cortisone	373	378	2.02	
L.R.	Cortisone	378	351	1.16	1.47
M.C.	Cortisone	360	350	2.13	0.63
P.E.	Cortisone	386	364	1.54	1.30
D.E.	Cortisone	340	366	0.64	2.95
Mean		365	366	1.61	1.93
±S.E.		±7.2	±4.9	±0.25	±0.56
Mean difference		+1		+0.41	
±S.E.		±8.6		±0.65	
P		>0.05		>0.05	
C.M.	Progesterone	332	376	1.2	2.4
A.B.	Progesterone	358	436	1.2	2.8
J.Y.	Progesterone	410	348	1.2	1.5

TABLE IV

PLASMA LEVEL OF Na AND Na-CLEARANCE BEFORE AND AFTER HORMONAL TREATMENT

Subject	Treatment	Plasma Na mg%		Na-Clearance ml/min	
		Before	After	Before	After
T.K.	DOCA	333.6	328.7	0.51	0.92
W.O'C.	DOCA	338.2	341.4	1.49	1.33
D.C.	DOCA	315.5	320.4	1.2	1.4
G.S.	DOCA	320.2	333.6	1.03	1.12
R.A.	DOCA	356.9	318.0	0.17	0.80
H.B.	DOCA	315.6	325.9	0.54	0.27
W.P.	DOCA	318.6	332.6	0.67	0.89
E.L.	DOCA	333.3	345.7	0.55	0.46
A.S.	DOCA	329.4	344.3	0.86	0.30
H.M.	DOCA	293.8	345.5	0.24	0.12
T.T.	DOCA	333.5	343.6	0.55	0.33
R.R.	DOCA	344.4	303.7		
Mean		327.8	331.9	0.72	0.72
±S.E.		±4.5	±3.8	±0.12	±0.14
Mean difference		+4.2		0	
±S.E.		±7.56		-	
P		>0.05			
R.F.	Cortisone	330	348	0.66	0.87
J.O'L.	Cortisone	323	323	1.17	
L.R.	Cortisone	318	326	0.58	0.68
M.C.	Cortisone	326	327	1.20	0.60
P.E.	Cortisone	335	302	0.88	0.79
D.E.	Cortisone	298	298	0.13	0.76
Mean		322	321	0.77	0.74
±S.E.		±5.3	±7.5	±0.17	±0.05
Mean difference		-1		+0.05	
±S.E.		±7		±0.20	
P		> 0.05		>0.05	
C.M.	Progesterone	333	331	0.3	0.9
A.B.	Progesterone	338	348	0.4	1.2
J.Y.	Progesterone	321	222	0.5	0.7

TABLE V

PLASMA LEVEL OF K AND K-CLEARANCE BEFORE AND AFTER HORMONAL TREATMENT

Subject	Treatment	Plasma K mg%		K-Clearance ml/min	
		before	after	before	after
R.A.	DOCA	16.6	12.2	16.2	
H.B.	DOCA	20.4	19.3	10.0	11.1
W.P.	DOCA	18.0	18.3	20.8	26.0
E.L.	DOCA	14.9	14.1	12.7	13.0
A.S.	DOCA	15.9	14.8	14.6	10.0
H.M.	DOCA	16.6	12.2	8.4	8.3
T.T.	DOCA	22.1	14.5	15.0	15.8
Mean		17.8	15.1	13.6	14.0
±S.E.		±1.0	±1.0	±1.8	±2.6
Mean difference		-2.7		+0.5	
±S.E.		±1.1		±1.2	
P		>0.02 <0.05		>0.05	
R.F.	Cortisone	15.8	16.4	11.1	12.3
J.O'L.	Cortisone	22.5	17.6	13.6	
L.R.	Cortisone	15.7	16.9	17.5	16.7
M.C.	Cortisone	14.0	14.0	31.0	5.4
P.E.	Cortisone	19.5	16.4	22.6	16.9
D.E.	Cortisone	12.0	11.7	9.0	21.6
Mean		16.6	15.5	17.5	14.6
±S.E.		±1.6	±0.9	±3.6	±2.7
Mean difference		-1.1		-3.7	
±S.E.		±1.0		±6.3	
P		>0.05		>0.05	
C.M.	Progesterone	14.3	15.1	24.9	35.5
A.B.	Progesterone	19.5	19.1	20.0	14.5
J.Y.	Progesterone	19.3	19.4	9.8	9.8

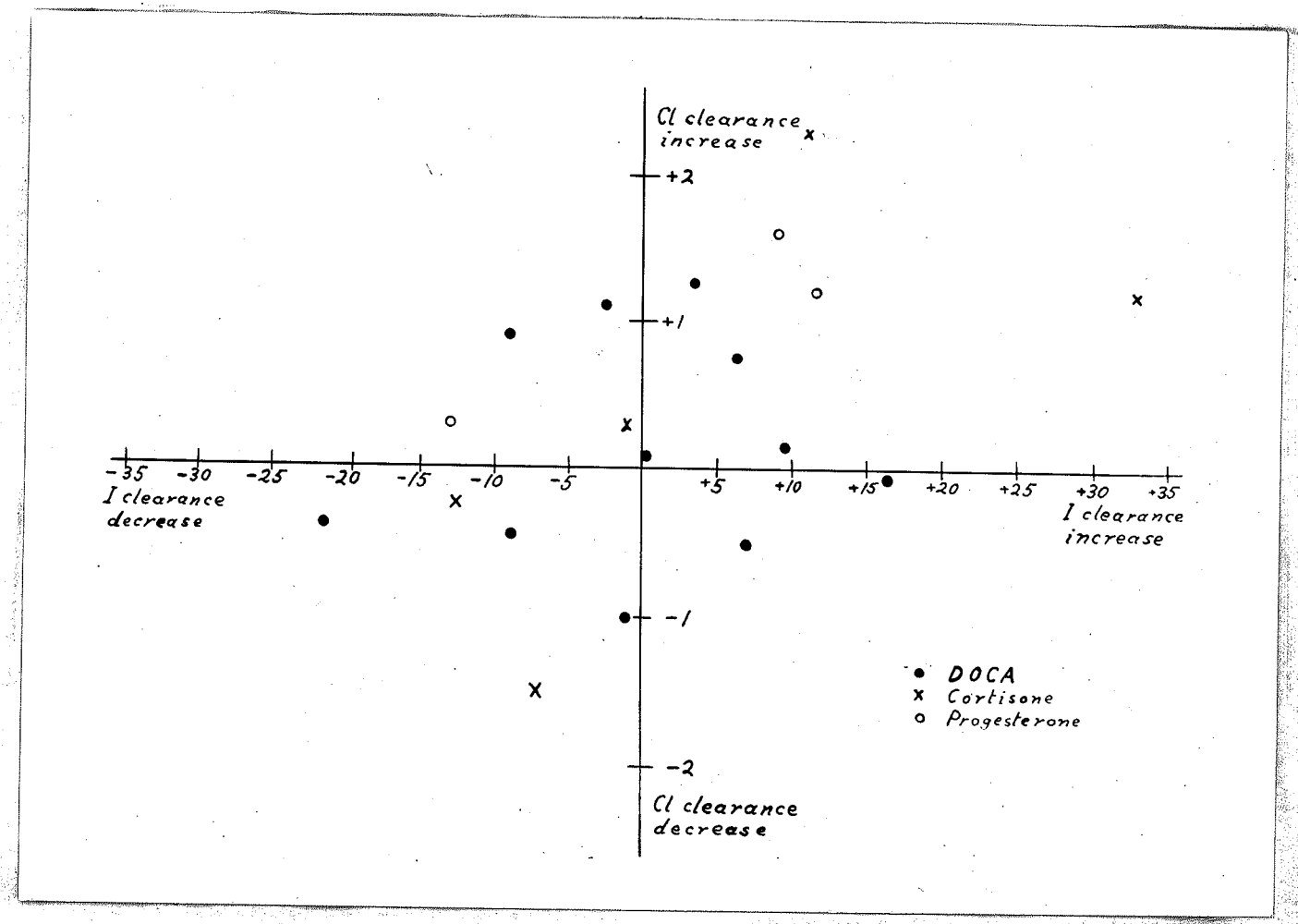

Fig. 1. Correlation between changes in Cl-clearance and I-clearance (ml/min) after treatment with DOCA, cortisone or progesterone for three days.

DISCUSSION

The majority of the subjects examined in this study were psychotic individuals. As far as the kidney function is concerned, there is no reason for believing that these patients reacted differently than normals. One patient with unusual drinking habits, which led to a very low urine flow, was not included in this report.

The endogenous creatinine clearance was used as an estimation of the glomerular filtration rate, having been shown to give values similar to those obtained with the inulin clearance (38,39). Brod and Sirota (38) mentioned that a difference between these two clearance values might appear under conditions of an increased protein breakdown. This possibility has to be kept in mind when the test is used in connection with ACTH or cortisone. A decrease of the average $\frac{\text{Creatinine clearance}}{\text{Inulin clearance}}$ ratio under treatment with ACTH or cortisone has been reported (18,25).

The endogenous creatinine clearance in these psychotic patients before any treatment was unusually widespread, even after standardization. The lowest value was 99 ml per minute, the highest 191 ml per minute. The reason for this variation is unknown.

It has been shown that DOCA increases the low filtration rate in patients with Addison's disease (43-45).

The findings in normals are less clear. Various observers report that DOCA caused an increased glomerular filtration rate in the dog (4,10,11,12). No change has been found in cats (4), in rats (9), and in men (46). ACTH and cortisone have been found usually to cause an increase in glomerular filtration rate in men (17,23-26,47,48).

As shown in Table I, marked changes in glomerular filtration rate can occur in a given individual after treatment with a steroid hormone. After DOCA the glomerular filtration rate appeared to rise somewhat and in four of five patients treated with cortisone, in whom the creatinine clearance could be determined, there was a decrease. However, a statistical analysis of these changes revealed no significant alterations in glomerular filtration rate after either DOCA or cortisone. In addition the fall in the endogenous creatinine clearance, observed in the patients following cortisone, might not be accompanied by a similar fall in inulin clearance and, therefore, might not be a true expression of changes in the glomerular filtration rate, as mentioned above. Levitt and Bader (23) report a gradual increase and later decrease of the glomerular filtration rate, measured as inulin clearance, under ACTH or cortisone therapy. The maximum increase was found 8-9 days after the onset of the

therapy, together with a significant increase of the volume of the extracellular space. In this series no determinations of the extracellular fluid volume were carried out. As reported in Part I, the drop in the total plasma protein concentration following DOCA is an indication of an increase in the plasma water. After cortisone and progesterone a similar change in plasma proteins was not observed. This latter finding is not in accord with the observations of Levitt and Bader and others (15,23). The time of examination was not the same, however.

No significant effects of DOCA, cortisone or progesterone on the renal clearance of iodide of chloride were noted. It thus seems clear that the previously reported inhibitory action of these steroids on the thyroid uptake of iodine is not a consequence of an increased renal disposal of iodine. Such an increased excretion of iodine after cortisone was reported by Frederickson et al (49); the time of examination, however, and the dosage of cortisone were different from this study.

In a given individual, marked alterations in the renal clearance of iodide or chloride can occur though not always paralleling one another, and such changes need not be due to a change in glomerular filtration rate.

The plasma level of stable iodine appeared to be increased after DOCA, but the difference proved to be insignificant on statistical analysis of the data. The before-mentioned plasma dilution which per se could cause a decrease of the iodine concentration has to be taken into account. The dilution cannot be accurately assessed quantitatively; the possibility of a significant increase of the total circulating iodine, however, cannot be ruled out. The slight decrease in the mean logarithmic plasma level of I^{131} after DOCA during the second clearance period might, therefore, be a dilution effect.

No retention of iodine occurred after administration of cortisone and no signs of plasma dilution were observed. The significant drop of the plasma level of radio-active iodine during the clearance period and 26 hours after the dose can thus not be explained as a dilution effect. The renal clearance is only insignificantly increased; an increased excretion is, therefore, not responsible for the lower plasma level of I^{131}. The true explanation of this decreased plasma I^{131} is not clear.

As mentioned above, no consistent changes in the plasma iodine were observed following progesterone.

Simultaneously obtained values concerning chloride, sodium and potassium showed surprisingly negative re-

sults. Apparently the plasma concentration and the renal clearance of sodium and chloride, examined three days after the onset of the hormonal treatment, do not differ significantly from the pre-treatment levels. No definite correlation between the individual changes in glomerular filtration rate and the tubular reabsorption of sodium was observed, contrary to the observation of Swisher et al (50).

It has to be kept in mind that the patients were not on a constant diet, which may explain some of the discrepancies between this and other studies. The importance of the sodium and chloride intake during electrolyte studies has recently been emphasized. (28)

There is a significant drop in the plasma concentration of potassium following DOCA. As the individual changes do not parallel the decrease in plasma protein concentration (Table II, Part I), the decreased potassium concentration seems not to be merely due to a plasma dilution. The potassium excretion and the renal clearance did not show a parallel increase. There are two possible explanations for this discrepancy. The patients received DOCA for three days and only on the fourth day the blood and urine was examined. It is possible that the excretion was elevated at first, to be followed later by a lower plasma level and subsequently by a secondary lowering of the excretion. Such a transient early increase of the potassium excretion during ACTH

or cortisone therapy has been described (21,47).

The other possibility would be a shift of potassium into the cells. An increased intracellular potassium concentration after DOCA has been reported (12,47), but since this increased concentration of cellular potassium was accompanied by a loss of intracellular water, an actual shift of potassium into the cells need not necessarily have occurred. In addition, since the absolute amount of intracellular potassium is increased in adrenalectomized animals (51) and adrenocortical tumors can cause a depletion of intracellular potassium (52,53), a shift of potassium into the cells following the administration of DOCA would seem rather unlikely.

A considerable number of papers deal with the influence of adrenal cortical hormones on electrolyte balance. The problem has been reviewed recently (54). The salt-retaining effect of DOCA in patients with Addison's disease (55,56) has been confirmed by many observers. The effects on normal men and normal animals are less clear. Earlier investigations (57-61) revealed usually a sodium retention after DOCA and an increased NaCl excretion after cortisone. The sodium-retaining effect has been confirmed (20,24,25) but no changes have been observed (19) and a case of sodium loss following DOCA is also reported (46). Cortisone has been claimed to act similarly to DOCA (62) and to act in an antagonistic

way (63,64). Studies on adrenal cortical hyperfunction (65-67) lead to the conclusion that in the normal the salt-retaining effect of DOCA is limited by other adrenal cortical hormones, possibly cortisone. In the course of cortisone therapy a retention of sodium and chloride was observed at first, which was followed by an increased excretion (14). The increased extracellular sodium has been explained solely on the basis of a shift of water, Na and Cl from the cells outward (15); the bones contain a considerable amount of mobile sodium and chloride (68).

Sex hormones are said to influence the electrolytes in a manner similar to the adrenal hormones (69-71). In this series progesterone has been studied, which has been claimed to prolong the life of adrenalectomized animals (70). As the chemical structure is very similar to that of DOCA, it is not unexpected that the action on the thyroid is comparable to that of DOCA and cortisone, as shown in Part I; but no definite conclusions can be drawn from this small group. The clearance rates of chloride and sodium seemed to be increased after the three-days' treatment with progesterone, but no consistent changes in the plasma levels were observed. It appears that the effect of progesterone on the electrolytes is not exactly identical with either DOCA or cortisone.

These investigations confirmed the observation that the kidneys excrete iodide more readily than chloride (72). After administration of DOCA, cortisone or progesterone

the excretion, tubular reabsorption and renal clearance of chloride and iodide may show a change; but the change does not always occur in the same direction for the two halogens and it is not necessarily of the same magnitude. Since the renal excretion of electrolytes normally is governed by adrenal cortical hormones to some extent, the theory that the kidney is unable to distinguish between halide ions has to be accepted with reserve.

SUMMARY AND CONCLUSIONS

The plasma level and the excretion of chloride, iodide, sodium and potassium has been studied in 21 subjects before and after a three-day treatment with desoxycorticosterone (10 mgm daily), cortisone (150-250 mgm daily), progesterone (25 mgm daily). Most of the changes induced were not significant. After DOCA an increase in plasma water, a decrease of the plasma potassium and possibly a slight retention of iodide has been found. Following cortisone an unexplained decrease in the level of radio-active iodine in plasma occurred. After progesterone an increase of the clearance rates of sodium and chloride is suggested. The renal clearance of I^{131} was not increased after administration of these hormones.

The chloride and iodide metabolism are not influenced in the same way by these hormones.

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PART III

THE THYROID FUNCTION IN SCHIZOPHRENIA

INTRODUCTION

In Part I, certain observations on the influence of various steroid hormones on the thyroid function were reported. Most of the subjects studied were patients on the psychopathic ward of the Winnipeg General Hospital, among them a number of schizophrenics.

In this present communication the results obtained in the first investigation of each schizophrenic patient - without any treatment - are compared with the results obtained with the same methods in non-schizophrenic patients and normals. All the patients were clinically euthyroid. Thirteen schizophrenics and fifteen non-schizophrenics were studied.

SUBJECTS AND METHODS

The subjects, their sex, age and diagnosis are listed in Tables I and II. The thyroid function was estimated by means of the uptake of radio-active and stable iodine, the thyroid clearance rate of I^{131} and the protein-bound iodine. The methods employed were the same as described in Part I.

TABLE I

SCHIZOPHRENIC PATIENTS

Subject	Sex	Age	Diagnosis	Thyroid Uptake I^{131} %/hr	Thyroid Uptake I^{127} µgm/hr	Thyroid Clearance ml/min	PBI µgm %
D.C.	M	22	Schizophrenia affective psychosis	5.5	3.3	30.5	2.3
R.A.	M	27	Schizophrenia, paranoid	1.7	2.7	7.1	4.2
A.S.	F	21	Schizophrenia affective psychosis	2.5	2.4	16.1	5.5
H.M.	F	21	Schizophrenia, paranoid	4.1	3.9	17.0	8.3
J.O'L.	M	32	Schizophrenia, paranoid	3.6	3.8	24.8	2.5
P.E.	M	39	Simple Schizophrenia	2.9	5.0	17.2	4.2
J.S.	M	17	Schizophrenia, catatonic	4.0	1.6	29.8	4.2
A.L.	M	43	Schizophrenia, paranoid	2.3	1.2	9.4	4.1
C.M.	M	23	Incipient Schizophrenia	2.2	1.8	7.1	4.0
S.M.	M	26	Simple Schizophrenia	2.9	-	19.0	4.3
J.M.	M	19	Schizophrenia, catatonic	2.6	-	20.6	2.7
C.S.	M	31	Schizophrenia, paranoid	4.5	3.2	37.6	2.7
V.R.	F	32	Simple Schizophrenia	1.6	0.4	5.6	6.6
			Mean	3.1	2.7	18.7	4.3
			±S.E.	±0.6	±0.6	±2.6	±0.4
			P value	>0.05	>0.05	>0.05	>0.05

TABLE II

NON-SCHIZOPHRENIC SUBJECTS

Subject	Sex	Age	Diagnosis	Thyroid Uptake I^{131} %/hr	Thyroid Uptake I^{127} µgm/hr	Thyroid Clearance ml/min	PBI µgm %
T.K.	M	18	Tuberculosis of ankle, Anthrodesis	1.7	1.8	10.6	4.9
W.O'C.	M	38	Psychosis with mental deficiency	3.6	1.1	21.8	3.5
G.S.	M	50	Mental deficiency with psychotic episodes	4.4	1.5	23.4	6.7
H.B.	F	41	Neurotic depressive reaction	5.7	2.7	24.2	4.8
W.P.	M	17	Primary Behaviour disorder	1.8	0.9	9.5	5.3
E.L.	F	22	Psychosis, mental deficiency	2.0	-	14.9	8.8
T.T.	M	31	Chronic alcoholism	2.3	2.3	11.5	7.0
R.R.	M	35	Parkinsonism, postencephalitic	3.5	-	20.6	5.0
R.F.	F	51	Rheumatoid arthritis	2.7	1.6	14.4	3.0
L.R.	M	39	Manic depressive, depressive	3.8	1.8	18.3	3.3
M.C.	M	31	Manic depressive, manic	4.2	2.7	22.1	3.6
D.E.	F	23	Psychoneurosis, anxiety state	6.2	1.6	31.9	4.5
W.M.	M	27	Chronic alcoholism	2.1	2.5	10.6	3.0
A.B.	M	49	Immature personality, emotional instability	1.5	1.8	8.0	3.8
J.Y.	M	19	Psychoneurosis, anxiety state	2.0	1.5	10.5	5.0
			Mean	3.2	1.8	16.8	4.8
			±S.E.	± 0.4	± 0.2	± 1.8	±0.4
Previously described group (12 subjects)			Mean	4.2	1.1	12.1	4.6
			± S.E.	± 0.6	± 0.2	± 2.5	±0.3
			P value	>0.05	> 0.02 < 0.05	> 0.05	>0.05

RESULTS

As may be seen in Tables I and II, there was no significant difference found between the two groups in the means of thyroid uptake of radio-active and stable iodine, thyroid clearance of I^{131} or protein-bound iodine. In Table II are also listed the means of these values reported in a previous communication from this laboratory (1). The uptake of stable iodine was lower in this latter group; no significant difference was found between the results of the other measurements.

DISCUSSION

Four different values estimating the thyroid function in a group of schizophrenic patients were found to be not statistically different from those obtained in a group of non-schizophrenics. The comparison of the latter group with a similar control group, investigated earlier in this laboratory, shows a significantly higher thyroid uptake of stable iodine in this study. This may be due to a different dietary intake. The patients who were examined in the previous

study were patients at the end of their hospital stay and were well-nourished, whereas in this group recent admissions to the psychopathic ward were examined whose diet may have been somewhat deficient in iodide before the admission.

Reiss et al (2), assuming a hyposensitivity of the tissues to thyroid hormone in schizophrenia, postulated an increased Thyrotrophin formation in the pituitary gland and thus a hyperactivity of the thyroid gland. Our data presents evidence that the thyroid function in patients suffering from schizophrenia does not differ significantly from that in normal controls. The observations of Bowman et al (3,4) are thus confirmed.

SUMMARY AND CONCLUSIONS

The thyroid function has been studied in thirteen schizophrenic patients and in fifteen non-schizophrenics by means of the thyroid uptake of radio-active and stable iodine, the thyroid clearance rate of I^{131} and the protein-bound iodine. No significant difference between the two groups has been observed.

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