

STUDIES IN STEROID METABOLISM. XX. THE REPRODUCIBILITY OF THE URINARY STEROID PATTERN IN HUMANS¹

By KONRAD DOBRINER²

THE DATA WERE ASSEMBLED AND THE MANUSCRIPT PREPARED BY:³

ATTALLAH KAPPAS,⁴ C. P. RHOADS AND T. F. GALLAGHER

(From the Laboratories of the Sloan-Kettering Institute for Cancer Research, New York, New York)

(Submitted for publication April 6, 1953; accepted May 29, 1953)

The most important problem that confronts an investigator concerned with a physiological process is the reproducibility of both the technique and the phenomenon under study. It is implicit in the investigation of steroid excretion that a given subject will exhibit a high order of reproducibility of his steroid pattern under comparable physiological conditions. Expressed in another way, steroid hormone production and metabolism as measured by the urinary excretion products should be reasonably constant for a normal individual. In the course of extensive studies of steroid metabolism in progress in this Institute, it has been possible to examine this problem and to demonstrate that in several subjects of different age and habitus the pattern of steroid excretion of a particular individual is reproducible with a high degree of precision.

METHODS

The methods employed in this laboratory for the fractionation, isolation, and identification of steroid metabolites have been published (1); the hydrolytic methods referred to are described in paper number XIX (2) in this series.

¹The authors gratefully acknowledge the assistance of grants from the American Cancer Society (on recommendation of the Committee on Growth of the National Research Council), the Commonwealth Fund, the Anna Fuller Fund, the Lillia Babbitt Hyde Foundation, and the National Cancer Institute of the National Institutes of Health of the United States Public Health Service.

²Konrad Dobriner died March 10, 1952.

³So far as we are aware, the interpretation of the data and the conclusions drawn are in essential agreement with the views held by the late Dr. Dobriner.

⁴Research Fellow of the American Cancer Society upon recommendation of the Committee on Growth of the National Research Council.

RESULTS

Replicate patterns, determined over varying periods of time, have been studied in nine normal male subjects; the initial, followed by the age, is descriptive of the subject. The steroid patterns in these subjects are listed in Table I. Crude ketosteroid data and the values for isolated compounds are listed in appropriate portions of the Table. Four compounds representing the major components of the α -ketonic fraction are listed; androsterone, etiocholanolone, 11-hydroxyandrosterone and 11-ketoetiocholanolone.

Subject C21: Patterns 1 and 2 were determined three months apart. Between these two periods, a course of intravenous ACTH was given for another study. A week intervened between the end of the ACTH period and the beginning of the urine collection for Pattern 2. There was no evidence of residual effect of the ACTH as determined by the metabolites studied.

Subject M21: Patterns 1 and 2 were determined under the same conditions and time limits as Subject C21.

Subject B21: Patterns 1 and 2 were obtained from successive long-term collections over a period of 10 months.

Subject Y27: Patterns 1 and 2 were determined on long-term urine collections separated by an interval of two years.

Subject N30: Patterns 1, 2, and 3 were determined within a period of two months.

Subject D31: Patterns 1, 2, 3, and 4 were determined within a five month period at approximately monthly intervals.

Subject K31: The details of Patterns 1 and 2 in this subject are similar to those of Subject R32.

TABLE I
Replicate steroid patterns in normal males

Compounds	Mg. per 24 hrs.										
11-Ketoetiocholanolone	1.1	1.0	.8	1.5	.5	.5	1.8	.9	.6	1.2	1.4
11-OH Androsterone	1.7	1.6	1.6	1.6	.1	.2	1.3	1.2	2.3	1.3	1.1
Etiocholanolone	6.0	5.9	7.6	6.3	2.9	2.5	7.9	6.0	3.2	3.7	3.1
Androsterone	6.2	7.6	7.0	5.9	1.0	1.1	3.5	2.5	2.5	2.7	3.6
% β of $\alpha + \beta$	7.7	12.4	4.5	2.6	2.6	5.9	8.3	12.2	6.5	5.0	6.6
β -Ketonic KS	1.6	3.1	1.1	.6	.2	.6	1.8	2.2	.8	.7	.9
α -Ketonic KS	19.3	22.2	23.5	22.1	7.6	9.5	19.8	15.8	11.6	13.2	12.7
Ketonic KS	23.7	24.9	24.3	26.9	7.7	11.8	23.1	22.0	15.3	15.0	16.3
Crude KS	29.8	31.5	28.8	32.7	20.3	34.4	23.3	22.2	19.1	24.6	21.3
Hydrolysis	D	D	D	D	B	B	A	A	A	A	A
Pattern number	1	2	1	2	1	2	1	2	1	2	3
Patient-Age	C21		M21*		B21		Y27		N30		

* This subject excreted 11-OH etiocholanolone in the following amounts during control periods: Period 1—.4 mg. and Period 2—.6 mg.

TABLE I—Continued

Compounds	Mg. per 24 hrs.										
11-Ketoetiocholanolone	.6	.8	.8	.7	.2	.3	.6	.8	.6	1.1	1.3
11-OH Androsterone	tr.	tr.	.3	tr.	1.0	.9	1.5	.9	.3	tr.	tr.
Etiocholanolone	2.9	2.1	2.1	2.0	1.8	1.9	3.1	3.8	4.9	8.9	10.1
Androsterone	1.7	1.3	1.2	2.0	1.8	1.9	2.5	1.7	1.8	2.9	3.5
% β of $\alpha + \beta$	3.2	3.7	3.9	2.8	20.2	13.0	6.1	4.5	1.6	1.3	1.2
β -Ketonic KS	.3	.4	.3	.2	1.9	.9	.7	.4	.2	.2	.2
α -Ketonic KS	9.2	10.5	7.5	7.0	7.5	6.3	.7	8.6	12.4	14.8	16.3
Ketonic KS	11.3	14.4	10.0	9.1	12.9	8.6	13.1	10.9	15.6	19.9	20.3
Crude KS	18.6	17.5	14.4	10.8	20.2	15.1	22.5	22.0	20.4	21.6	23.2
Hydrolysis	A	A	A	A	C	C	C	C	A	A	A
Pattern number	1	2	3	4	1	2	1	2	1	2	3
Patient-Age	D31			K31			R32			T42	

Subject R32: Patterns 1 and 2 were determined three months apart. During the intervening period, a course of intramuscular injections of ACTH was given for another study. Pattern 2 followed the cessation of ACTH by an interval of two weeks.

Subject T42: Patterns 1, 2 and 3 were determined at one month intervals.

DISCUSSION

These data are presented initially in this series for two purposes: 1) To demonstrate the degree of reproducibility of techniques employed in the extensive studies to be presented later. 2) To show clearly that without the stimulus of acute or chronic pathologic or metabolic change, as exemplified by disease, hormonal therapy, etc., steroid excretion tends to vary only within narrow limits. The determinants of these limits are as yet unknown.

SUMMARY

Data are presented that indicate a high order of constancy in the production, metabolism, and

excretion of steroid hormones as determined by isolation and quantitation of individual hormonal metabolites.

ACKNOWLEDGMENTS

The authors wish to express their appreciation to the large group of devoted Research Assistants and Technicians who made much of the work possible. The routine chemical and chromatographic separations were carried out by a group under the supervision of Madeleine Stokem and Ruth Jandorek. The colorimetric analyses were under the supervision of Olga Teager. The infrared spectrometry was under the supervision of Friederike Herling.

REFERENCES

- Dobriner, K., Lieberman, S., and Rhoads, C. P., Studies in steroid metabolism. I. Methods for the isolation and quantitative estimation of neutral steroids present in human urine. *J. Biol. Chem.*, 1948, 172, 241.
- Dobriner, K., Studies in steroid metabolism. XIX. The α -ketosteroid excretion pattern in normal males. *J. Clin. Invest.*, 1953, 32, 940.