Table I. Deamination of some amino acids and amines on their incubation with 'transformed' beef liver mitochondrial amine oxidase.

Substrates and their concentrations	$M \times 10^{-3}$	V_{max} values (mμmoles of NH_3/mg of protein/min) mean values ± S.E.	
Histamine · HCl	10	2.8 ± 0.6	(3)
Histidine · HCl	10	0	(4)
Cadaverine · 2 HCl	10	2.5 ± 0.2	(4)
L-Lysine · HCl	15	1.5 ± 0.07	(8)
α-Hippuril-L-lysine	10	2.2 ± 0.1	(3)
α-Carbobenzoxy-lysine[11]	10	0.95, 0.47	(2)
ε-Carbobenzoxy-lysine[11]	10	0 0	(2)
L-Ornithine	5	1.7 ± 0.1	(4)
γ-Aminobutyric acid	20	1.9 ± 0.4	(5)
α-Aminobutyric acid	10	0	(4)
β-Alanine	10	1.3 ± 0.2	(5)
α-Alanine	10	0	(3)

Composition of samples and experimental conditions as described[6]. Number of experiments in brackets.

Table II. Effect of β-aminopropionitrile fumarate on the activity of 'transformed' rat liver mitochondrial amine oxidase.

Concentrations of the inhibitor ($M \times 10^{-3}$)	Inhibition of deamination (%) (mean values from the data of 4–6 parallel assays)		
	lysine	serotonin	γ-ABA
1.0	100	9.5	–
0.1	100	11.5	5.0
0.01	45.5	–	12.0

Composition of samples as described[6]. The inhibitor[12] was preincubated at room temperature with the enzyme preparations for 30 min before the addition of one of the substrates in following concentrations ($M \times 10^{-3}$): serotonin creatinine sulphate (5), DL-lysine·HCl (15), γ-aminobutyric acid (ABA) (20); in control samples (without the inhibitor) deamination rates were respectively: 2.47, 1.71, 0.99 mμmoles of NH_3mg of protein/min.

deamination. Deamination of lysine on incubation with 'transformed' mitochondrial amine oxidase is completely inhibited by $10^{-4}M$ β-aminopropionitrile while its inhibitory effect on deamination of other substrates of the enzyme (serotonin and γ-aminobutyric acid) is negligible (Table II).

It is noteworthy that the activity of 'transformed' mitochondrial amine oxidase is not inhibited by high concentrations of conventional monoamine oxidase inhibitors[6] which do not produce experimental lathyrism[13].

Выводы. «Трансформированная» митохондриальная аминоксидаза катализирует отщепление ε-аминогруппы лизина. Эту реакцию избирательно тормозит латирогенный агент β-аминопропионитрил.

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Interconversion of Cortisol and Cortisone in the *Macaca mulatta*

The principle corticosteroids present in mammalian blood are cortisol, corticosterone and aldosterone[1–7]. Although small amounts of 11-desoxy-17α-hydroxycorticosterone (pregn-4-ene-17α, 21-diol-3-one), 11-dehydrocorticosterone (pregn-4-ene-21-ol-3, 11-dione), cortisone (pregn-4-ene-17α, 21-diol-3, 11-dione), and 11-desoxycorticosterone (pregn-4-ene-21-ol-3-one) have been detected in blood, their concentrations in blood have not been established[8,9]. Of these steroids, cortisol is considered to be the physiologically active glucocorticoid in man. The efficacy of cortisol in affecting thymus involution, liver glycogen deposition and anti-inflammatory response exceeds that of cortisone[10]. Furthermore, cortisol in vitro markedly inhibited the glucose uptake by rat thymus cell suspension while cortisone was ineffective[11]. Since the 11β-hydroxysteroid dehydrogenase activity is low in the thymus[12], this finding supports the proposition that cortisol is the active agent and the biological efficacy of cortisone is dependent upon its conversion to cortisol. On the other hand, KOIKE et al.[13] demonstrated that the protein synthetic activity of polysomes from livers of cortisone-treated rats was greater than that of cortisol-treated rats. These seemingly divergent results suggest that cortisol and cortisone may be active depending on the tissue or assay systems used, or that a balance of these steroids may be of importance for their biological efficacy. This study was conducted to observe the interconversion of these 2 steroids in vivo in the *Macaca mulatta* and to establish the relative levels of these steroids in blood.

Material and methods. 1, 2-^{3}H-cortisol and 1, 2-^{3}H-cortisone with specific activities of 22 and 36 c/mmole were

purchased from New England Nuclear Corp., Boston, USA. Chromagram 606 was purchased from Eastman Kodak Co., Rochester (USA). The steroids were purified on silica gel chromatogram before use.

Administered were 10 μc of ^{3}H-cortisol (0.45 nmole) and ^{3}H-cortisone (0.27 nmole) in ml of saline i.v. to an adult female monkey (*M. mulatta*) weighing 8.0 kg. Blood samples were collected in heparin at 15 and 60 min intervals, centrifuged at 600 *g* for 15 min and the plasma thus separated from the cells. The plasma was extracted 3 times with an equal vol. of methylene chloride. The extracts were pooled and evaporated to dryness. The red cells were washed 3 times with an equal vol. of saline. The saline washings were pooled and extracted with methylene chloride. The methylene chloride extract was evaporated to dryness. The remaining red cell fraction was hemolyzed in 2 vol. of distilled water. The hemolysate was extracted 3 times with an equal vol. of methylene chloride. The methylene chloride extracts were pooled and evaporated. The residues obtained from the methylene chloride extracts were dissolved in 0.1 ml of ethanol and subjected to silica gel chromatography. The chromatogram was developed with a solution containing chloroform: ethanol, 96:4, v/v, at room temperature for 45 min, dried, cut into cm-strips and extracted with ethanol. The ethanol fraction was evaporated and the residue dried at 90 °C for 30 min. 10 ml of phosphor in toluene was added and the samples were counted in a Packard Tri-Carb liquid scintillation spectrometer, model 3003. The average efficiency for tritium was found to be 18%, which was used in the calculation.

Results and discussion. The Table shows the radioactive counts in the various fractions of blood at 15 and 60 min following the i.v. administration of ^{3}H-cortisol and ^{3}H-cortisone. The total counts in blood were greater with ^{3}H-cortisol than with ^{3}H-cortisone. This is in accord with the reports that the biological half-time of cortisol in blood of human patients was 114 ± 6.5 min (90–130 min) and that of cortisone was about 60–65 min[14].

The distribution of ^{3}H-cortisol in the plasma, saline washings and red cells was 64, 24 and 12%, respectively, at 15 min and 61, 30 and 9%, respectively, at 60 min. With ^{3}H-cortisone, it was 70, 28 and 2%, respectively, at 15 min and 76, 22 and 2%, respectively, at 60 min. The greatest concentration of labelled steroids was found in the plasma. This is in accord with the reports that cortisol is principally bound to transcortin and albumin in blood[15]. Following ^{3}H-cortisone administration, the amount of labeled steroids remaining in RBC after saline washing was low and was not feasible to count upon separation by chromatography. This finding indicates that the rapid disappearance of cortisone was not dependent upon its incorporation into red cells.

The ratio of cortisone to cortisol in plasma (Table) was approximately 0.25 following ^{3}H-cortisol administration which was attained within 15 min; whereas, with ^{3}H-cortisone it was 0.41 after 1 h. This finding indicates that cortisol was converted to cortisone and reached a steady state rapidly. The conversion of cortisone to cortisol was slower. The variation in the contents of E and F in plasma, saline washings and RBC suggests that the steroid adsorbed to and incorporated into RBC is not a reflection of the plasma levels. The constant ratio of E to F may be of importance in the regulation of tissue metabolism by glucocorticoids[16].

Zusammenfassung. Die Umwandlung von Kortisol in Kortison und umgekehrt wird nach Injektion von radioaktiven Steroiden bei einem weiblichen Affen (*Macaca mulatta*) untersucht. Es konnte festgestellt werden, dass im Blut Kortisol relativ rasch in Kortison umgewandelt wurde, während umgekehrt Kortison wesentlich langsamer umgewandelt wird.

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Blood levels following administration of ^{3}H-cortisol and ^{3}H-cortisone

Fractions	Time after administration (min) 15 cpm	E:F	60 cpm	E:F
(A) ^{3}H-cortisol				
Plasma	9,100	0.24	7,450	0.22
	8,500	0.26	7,150	0.24
Saline washings	3,450	0.63	3,500	0.54
	3,150	0.59	3,700	0.58
Red cells	1,300	0.44	1,100	0.37
	1,700	0.48	1,100	0.36
Total count	13,850	–	12,050	–
	13,950	–	11,950	–
(B) ^{3}H-cortisone				
Plasma	4,350	0.71	3,650	0.42
	4,450	0.69	3,550	0.40
Saline washings	1,800	0.60	900	0.38
	1,750	0.66	1,100	0.42
Red cells	110	–	100	–
	80	–	100	–
Total count	6,260	–	4,650	–
	6,280	–	4,750	–

E:F, cortisone:cortisol.

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