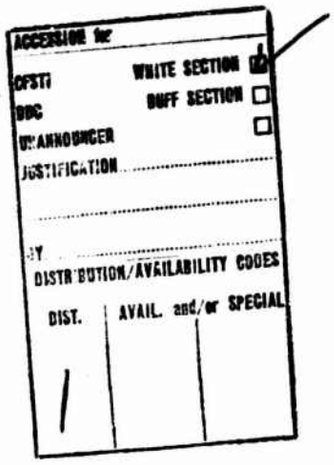
SAM-TR-68-24

ENDOCRINE-METABOLIC EFFECTS OF UNUSUALLY LONG OR FREQUENT FLYING MISSIONS IN C-130E OR C-135B AIRCRAFT

HENRY B. HALE, Ph.D., et al.

USAF School of Aerospace Medicine
Aerospace Medical Division (AFSC)
Brooks Air Force Base, Texas

March 1968



ENDOCRINE-METABOLIC EFFECTS OF UNUSUALLY LONG OR FREQUENT FLYING MISSIONS IN C-130E OR C-135B AIRCRAFT

HENRY B. HALE, Ph.D.*
CLARENCE A. ANDERSON, Captain, USAF, MC†
EDGAR W. WILLIAMS, B.A.*
EMANUEL TANNE, Captain, USAF, MC†

*Physiology Branch, USAF School of Aerospace Medicine, Brooks Air Force Base, Tex.
†Office of Command Surgeon, Military Airlift Command, Scott Air Force Base, Ill.

FOREWORD

This research was conducted jointly by the Office of the Command Surgeon, Military Airlift Command, and the Physiology Branch, USAF School of Aerospace Medicine, the latter group working under task No. 775801. The field phase was performed at various times in the period beginning in November 1964 and ending in December 1965. The laboratory and statistical phases of this research were completed late in 1966. This report was submitted for publication on 18 December 1967.

Acknowledgment is made of the contributions of analytical chemists--Technical Sergeant H. M. Avery, Jr., J. K. Farquhar, J. B. Garcia, Jr., J. A. Gonzales, R. E. Miranda, and Airman First Class R. W. Prettyman; of statisticians in the Biometrics Branch—R. C. McNee, R. B. Nivison, Jr., and Senior Master Sergeant J. I. Clogston; and of MAC coordinators—Colonel M. Nareff, Colonel S. O. Smelsey, Major C. L. Mayhew, Major H. H. Fry, Jr., Major R. J. Salina, and Captain J. W. White, Jr.

This report has been reviewed and is approved.

GEORGE E. SCHAFER
Colonel, USAF, MC
Commander

ABSTRACT

Flight-stress appraisal was made by means of a battery of urinary determinations (epinephrine, norepinephrine, 17-OHCS, urea, uric acid, phosphorus, magnesium, sodium, and potassium) for flyers who participated in (a) 20-hour missions in C-130E aircraft (flights from New Zealand to Antarctica, and back), (b) 6-day missions in C-135B aircraft (earth-circling missions), or (c) 7-week missions in C-135B aircraft (over-frequent transoceanic and transcontinental flying). The adrenal medulla (as judged by urinary epinephrine) consistently showed flight-sensitivity, but other endocrine-metabolic functions varied in ways indicative of adaptation. With flight circumstances standardized (particularly with respect to time of day), flight effects tended to be reproducible. With crew rest limited to 2 days, recovery from flight-stress tended to be incomplete. Sleep deprivation and crew position were shown to be factors which modify flight-stress reactions. Eastbound and westbound earth-circling missions did not induce different degrees of flight-stress, as judged by these endocrine-metabolic indices.

ENDOCRINE-METABOLIC EFFECTS OF UNUSUALLY LONG OR FREQUENT FLYING MISSIONS IN C-130E OR C-135B AIRCRAFT

I. INTRODUCTION

In studies (2, 4, 7, 8) conducted in the Physiology Branch of the USAF School of Aerospace Medicine, flight-stress assessment by means of a battery of urinary determinations has been shown to be feasible. This battery provides information on sympathoadrenal, adrenocortical, and metabolic activities. At the request of Brigadier General Harold F. Funsch, Surgeon, Military Airlift Command, this method of flight-stress appraisal was utilized in four flying exercises in which the flying operations were either unusually long or frequent, or both. This report presents the findings in these different studies.

II. METHODS

One-day mission

Urine specimens were collected from crewmembers of C-130E aircraft shortly after completion of flights from Christchurch, New Zealand, to McMurdo Station, Antarctica, and back. Typically, these flights began between 1000 and 1200 hours, and each leg of the flight lasted approximately 8 hours, with ground time at McMurdo Station amounting to 2 or 3 hours. Duty time on the days of these flights, including preflight time, usually amounted to 20 or more hours. These studies were run in November and December in two successive years. In the first year, determinations were made only on pilots (aircraft commanders and copilots); in the second year, data were obtained for pilots, flight engineers, navigators, and loadmasters. There were 10 subjects in year I and 47 subjects in year II. In year I, control determinations were made 7 to 10 days after the test flights, and there was little or no flying in the intervening period. In year II, control determinations were made 2 days after the flights. The time of day at which the control urine specimen was collected for each subject was the same as that for his postflight specimen.

Six-day mission

Urine specimens were collected from pilots (aircraft commanders, 1st pilots, and 2d pilots) of C-135B aircraft shortly after completion of eastbound or westbound earth-circling flying missions ("Embassy Runs"). The eastbound missions usually began at 2000 hours on a particular day of the week (Friday) and usually ended at 1500 hours on the following Thursday. Total flying time approximated 44 hours, and total crew rest time approached 96 hours. The westbound missions usually began at 1400 hours on Monday and usually ended at 2100 hours on the following Saturday. Total flying time approximated 48 hours, and total crew rest time approached 78 hours. Urine specimens were collected shortly after completion of each mission and again at the corresponding time 2 days later.

The legs of the eastbound mission were as follows: (a) Travis AFB, Calif., to Charleston AFB, S.C. (flight time = 5 hours; ground time = 15 hours); (b) Charleston AFB to Torrejon AB, Spain (flight time = 8.3 hours; ground time = 23 hours); (c) Torrejon AB to Dhahran, Saudi Arabia (flight time = 6.5 hours; ground time = 2 hours); (d) Dhahran to Karachi, Pakistan (flight time = 2.5 hours;

ground time = 2 hours); (e) Karachi to New Delhi, India (flight time = 1.7 hours; ground time = 15 hours); (f) New Delhi to Bangkok, Thailand (flight time = 3.7 hours; ground time = 2 hours); (g) Bangkok to Saigon, South Vietnam (flight time = 1.5 hours; ground time = 2 hours); (h) Saigon to Clark AB, Philippine Islands (flight time = 2 hours; ground time = 19 hours); (i) Clark AB to Hickam AFB, Hawaii (flight time = 8.5 hours; ground time = 24 hours); and (j) Hickam AFB to Travis AFB, Calif. (flight time = 4.5 hours).

The legs of the westbound mission were as follows: (a) Travis AFB to Hickam AFB (flight time = 4.8 hours; ground time = 15 hours); (b) Hickam AFB to Clark AB (flight time = 10.5 hours; ground time = 24 hours); (c) Clark AB to Saigon (flight time = 2.2 hours; ground time = 2 hours); (d) Saigon to Bangkok (flight time = 1.3 hours; ground time = 2 hours); (e) Bangkok to New Delhi (flight time = 4 hours; ground time = 15 hours); (f) New Delhi to Karachi (flight time = 1.7 hours; ground time = 2 hours); (g) Karachi to Dhahran (flight time = 2.5 hours; ground time = 2 hours); (h) Dhahran to Torrejon AB (flight time = 7 hours; ground time = 24 hours); (i) Torrejon AB to Charleston AFB (flight time = 8.6 hours; ground time = 2 hours); and (j) Charleston AFB to Travis AFB (flight time = 5.2 hours).

Seven-week mission

Commanders of C-135B aircraft were studied, by means of urinalysis, during an exercise of 7 weeks' duration which required unusually frequent flying over a circuit extending from Japan to Spain. Urine specimens were collected shortly after completion of transatlantic flights or transpacific flights (average duration = 10 hours). Representative subjects were studied in the early weeks of the exercise; others were studied in the later weeks; and still others were studied 7 to 10 days after the end of the exercise. As an additional phase of the study, aircraft maintenance personnel were studied repeatedly during this same exercise, using urine specimens collected in the 1st, 3d, and 6th weeks of the exercise and 1 week after termination of the exercise, with time of day standardized at 1600 hours.

Analytical technics

The urine specimens were collected into dilute HCl and promptly frozen. At the completion of each exercise, all urine specimens were shipped in the frozen state to the laboratory, where they were analyzed for creatinine, uric acid, urea, phosphorus, potassium, and sodium (all measured by means of the Technicon AutoAnalyzer), magnesium (11), total 17-hydroxycorticosteroids (10), and two catecholamines—norepinephrine, and epinephrine (1). As timed urine collections were impractical under these circumstances, each urinary constituent has been expressed as a creatinine-based ratio, rather than as hourly excretion rate. Analysis of variance was the method employed in evaluating these data.

III. RESULTS

One-day mission

Statistical appraisal of the two sets of urinary data for the 10 flyers studied in the first year of the New Zealand–Antarctica flying missions revealed significant variation for only five variables—namely, norepinephrine ($P < .05$), epinephrine ($P < .01$), the ratio of norepinephrine to epinephrine ($P < .001$), urea ($P < .01$), and the ratio of sodium to potassium ($P < .025$). Each of these variables, with the exception of the norepinephrine/epinephrine ratio (NE/E), indicated that physiologic activity was higher under flying conditions than under control (nonflying) conditions. The change in the NE/E ratio evidently indicates that flight had a differential effect on the two parts of the sympathoadrenal system.

Eight of the subjects completed their flights in a nighttime period (0300 to 0600 hours), while the remaining 2 subjects completed theirs in the afternoon (at 1700 hours). Since most of the urinary variables under study

ordinarily undergo circadian fluctuation, pooling of data obtained at such widely separated times of day is disadvantageous. Re-evaluation was therefore made with the group reduced to the 8 subjects whose flights ended in the nighttime period. Mean values for this group are presented in table I. There was significant variation for epinephrine ($P < .025$), the NE/E ratio ($P < .005$), 17-hydroxycorticosteroids (17-OHCS) ($P < .05$), uric acid ($P < .005$), and urea ($P < .05$). For the purpose of assuring proper perspective, laboratory control (baseline) data have been included in the table. These baselines were established in a study of 12 members of the laboratory staff, each man collecting one urine specimen per week over an entire year, with the time of day standardized at 0630 hours.

The 8-man group of flyers, when studied under control conditions (normal nighttime sleep, without any flying activity in the preceding daytime period), had near baseline values for norepinephrine, epinephrine, and the NE/E ratio. These results, along with the finding that the postflight norepinephrine and epinephrine values for the flyers were high relative to their own control values, permit the conclusion that flight had a stimulatory influence on the sympathoadrenal system. There is also evidence that flight affected the two parts of this system unequally, as the postflight norepinephrine value amounted to 159% of the group's own control value, while that for epinephrine was greater, amounting to 260%. The reduction in the NE/E ratio from the control level of approximately 6:1 to the postflight level of approximately 3:1 obviously is a reflection of this differential flight effect. The NE/E ratio, by combining the flight effects on the individual catecholamines into a single measure, becomes an unusually sensitive flight-stress index.

Apart from the catecholamine indications, there was little evidence of flight-induced endocrine-metabolic change, the postflight

TABLE I

Effects of nighttime C-130E flights

Urinary variable*	Year I		Year II		Laboratory control (12)
	Postflight (8)†	Control (8)	Postflight (18)	Control (18)	
Norepinephrine, μg.	3.62	2.27	3.64	4.30	2.64
Epinephrine, μg.	1.09	0.42	0.94	1.20	0.51
Ratio: NE/E	3.4	5.8	4.4	4.2	5.4
17-OHCS, μg.	211	424	190	198	121
Uric acid, mg.	28	35	34	37	29
Urea, mg.	1,218	998	1,223	1,156	1,158
Phosphorus, mg.	48	43	46	54	60
Magnesium, mEq.	0.40	0.44	0.34	0.45	0.49
Potassium, mEq.	2.1	3.0	2.6	3.1	2.0
Sodium, mEq.	7.4	6.2	7.5	8.1	7.9
Ratio: Na/K	3.8	2.2	3.0	3.1	4.3
Volume, ml.	54	54	63	101	51

*Except where otherwise indicated, each urinary variable is a creatinine-based ratio (quantity/100 mg. creatinine).
†Number in parentheses is number of subjects.

values for 17-OHCS, uric acid, urea, magnesium, potassium, sodium, Na/K, and urine volume all approaching the respective baselines. Phosphorus was exceptional, falling considerably below its baseline. Under control conditions, the flyers again showed general agreement with the baselines; however, as exceptions, 17-OHCS and uric acid values were relatively high, while the values for urea and the Na/K ratio were relatively low. This finding of relatively high 17-OHCS and uric acid excretion, along with the unusual Na/K ratio, under what was thought to be a stress-free circumstance, raises questions regarding the worth of these data for control purposes. These three changes are common to all types of stress.

Table I also includes data for 18 members of crews who flew New Zealand–Antarctica missions in the second year. These particular flyers completed their flights in the same nighttime period (0300 to 0600 hours) as the previously mentioned group, and they show close agreement in their postflight urinary values with the other group. Evidently, with the flying circumstances essentially standardized, the physiologic responses were reproducible. This intergroup agreement in postflight values is even more impressive when it is noted that, under control conditions, these groups show considerable disagreement. This latter disagreement appears to relate to the length of the crew rest periods. In year II, in which the period was only 2 days, the control values did not differ statistically from the postflight values, which indicates that flight effects were persistent. In year I, in which the intervals were as long as 10 days, there was significant variation between certain postflight and control values, as was mentioned earlier. The conclusion is that recovery involved slow reversal of certain of the flight-induced changes and possibly some overcorrection ("rebound").

Table II presents the individual data for the 2 flyers in year I who completed their Antarctic flight in the afternoon because of a 15-hour delay caused by bad weather. Laboratory control data have been added to assure proper perspective. This laboratory group consisted

TABLE II

Effects of daytime C-130E flights

Urinary variable*	Pilot A		Pilot B		Laboratory control
	Postflight	Control	Postflight	Control	
Norepinephrine, μg.	9.28	3.46	9.41	1.46	2.94
Epinephrine, μg.	1.95	0.55	2.80	0.35	0.78
Ratio: NE/E	4.7	6.4	3.4	4.2	3.7
17-OHCS, μg.	321	234	420	212	358
Uric acid, mg.	40	37	64	20	40
Urea, mg.	1,590	1,211	1,206	821	1,208
Phosphorus, mg.	53	71	45	63	54
Magnesium, mEq.	0.82	0.46	1.53	0.45	0.39
Potassium, mEq.	2.7	1.7	2.9	1.9	4.8
Sodium, mEq.	10.2	2.1	12.5	1.1	9.0
Ratio: Na/K	3.7	1.2	4.3	0.6	2.2
Volume, ml.	227	90	125	34	81

*Except where otherwise indicated, each urinary variable is a creatinine-based ratio (quantity/100 mg. creatinine).

of 26 staff members who were performing accustomed laboratory or office work. The time of urine collection agreed with that for the 2 flyers. These particular flyers show, in their excretion pattern, signs of flight-stress of very high degree. For example, their postflight norepinephrine values amounted to 268% and 644% of their own control values, while their epinephrine values amounted to 354% and 800%. Additionally, their postflight values for 17-OHCS, uric acid, urea, magnesium, potassium, sodium, Na/K, and urine volume were all high relative to their own control values, and their NE/E and phosphorus values were both relatively low. Under control conditions, both of these flyers had urinary values that approached those of the laboratory controls, and there is also some evidence of over- or undershooting. For example, epinephrine and 17-OHCS values both fell below the respective baselines, while the NE/E ratio and phosphorus both overshot their respective baselines.

Additional data for year II are presented in table III. The data have been organized to give a forenoon group (0700 to 1200 hours), an evening group (1800 to 2300 hours), and a night group (0300 to 0600 hours). The data for the latter group also appear in tables I and V, where they serve other purposes. The control and postflight data for these different groups of flyers have been plotted against time of day in figure 1 in order to bring out the character of the time trends and to emphasize that most of the paired curves showed parallelism. The data for the laboratory controls have also been incorporated into curves which appear along with those for the flyers. There are cases of parallelism and also of nonparallelism between curves for the flyers and the nonflyers.

The possibility that crew position was a factor contributing to flight-stress was also investigated, using data obtained in year II. With all of the daytime and nighttime data pooled, some differences were found for crew positions (table IV). Analysis of variance established significant relationship to crew position for epinephrine ($P < .05$), the NE/E ratio ($P < .005$), and the Na/K ratio ($P < .05$). The pilots and flight engineers showed very close agreement in their average epinephrine excretion and in their urinary NE/E values; and in both respects, these particular groups were clearly differentiated from the navigators and loadmasters (and from the laboratory controls). In turn, there is near agreement in both respects with the results obtained for pilots in year I. The flight engineers are differentiated from all others by having a relatively low Na/K ratio.

To determine whether the nighttime Antarctic flights were unusually stressful, comparison was made (table V) with data for crewmembers of C-130E aircraft who, after a prolonged crew rest in Hawaii, flew by way of Pago Pago, Samoa, to Christchurch, New Zealand, completing their flights at 0600 hours. Their postflight values tend to agree with those for the 18 whose flights from Antarctica to Christchurch also ended late at night. It is therefore concluded that the Antarctic flight was not unusually stressful. Of interest is the finding that the flight effects tended to be persistent in both groups. In both cases, the crew rest period was 2 days.

Six-day mission

Data for the pilots who flew the 6-day global missions are presented in table VI. Technical difficulties prevented catecholamine determinations for these subjects. The times of day at which the missions were completed ranged from 1500 to 2300 hours. Flight direction was one of the factors considered in the analysis of variance, but there was no evidence of physiologic difference between westbound and eastbound groups; so all data were pooled. Table VI presents mean values for 27 subjects (13 flew eastbound missions, and 14 flew westbound missions). For 24 of these men, preliminary observations were made 1 day before the start of the mission, with time of day the same as the expected time of mission completion. In most respects, the flyers' preflight and control values tended to agree, and in turn there was essential agreement with the laboratory control values. The postflight and control values for the 27 flyers did not differ statistically. It is therefore concluded that the 6-day

TABLE III

Flight-stress in relation to time of day

Urinary variable*	0700 to 1200 hours			1800 to 2300 hours			0300 to 0600 hours		
	Postflight (17)†	Control (17)	Lab control (26)	Postflight (12)	Control (12)	Lab control (26)	Postflight (18)	Control (18)	Lab control (12)
Norepinephrine, μg.	6.12	7.17	2.72	5.23	5.56	3.03	3.64	4.30	2.64
Epinephrine, μg.	1.59	1.86	0.60	1.26	1.36	0.82	0.94	1.20	0.51
Ratio: NE/E	4.2	4.2	4.6	4.5	4.8	3.7	4.4	4.2	5.4
17-OHCS, μg.	382	472	439	264	270	326	190	198	121
Uric acid, mg.	44	43	42	42	46	38	34	37	29
Urea, mg.	1,377	1,329	1,211	1,197	1,199	1,237	1,223	1,156	1,158
Phosphorus, mg.	43	46	29	51	51	60	46	54	60
Magnesium, mEq.	0.42	0.52	0.36	0.31	0.42	0.47	0.34	0.45	0.49
Potassium, mEq.	4.1	4.4	6.2	3.6	3.3	4.5	2.6	3.1	2.0
Sodium, mEq.	10.1	10.2	9.6	11.9	10.1	9.2	7.5	8.1	7.9
Ratio: Na/K	2.7	2.4	1.7	3.8	3.5	2.5	3.0	3.1	4.3
Volume, ml.	101	115	87	98	109	90	63	101	51

*Except where otherwise indicated, each urinary variable is a creatinine-based ratio (quantity/100 mg. creatinine).
†Number in parentheses is number of subjects.

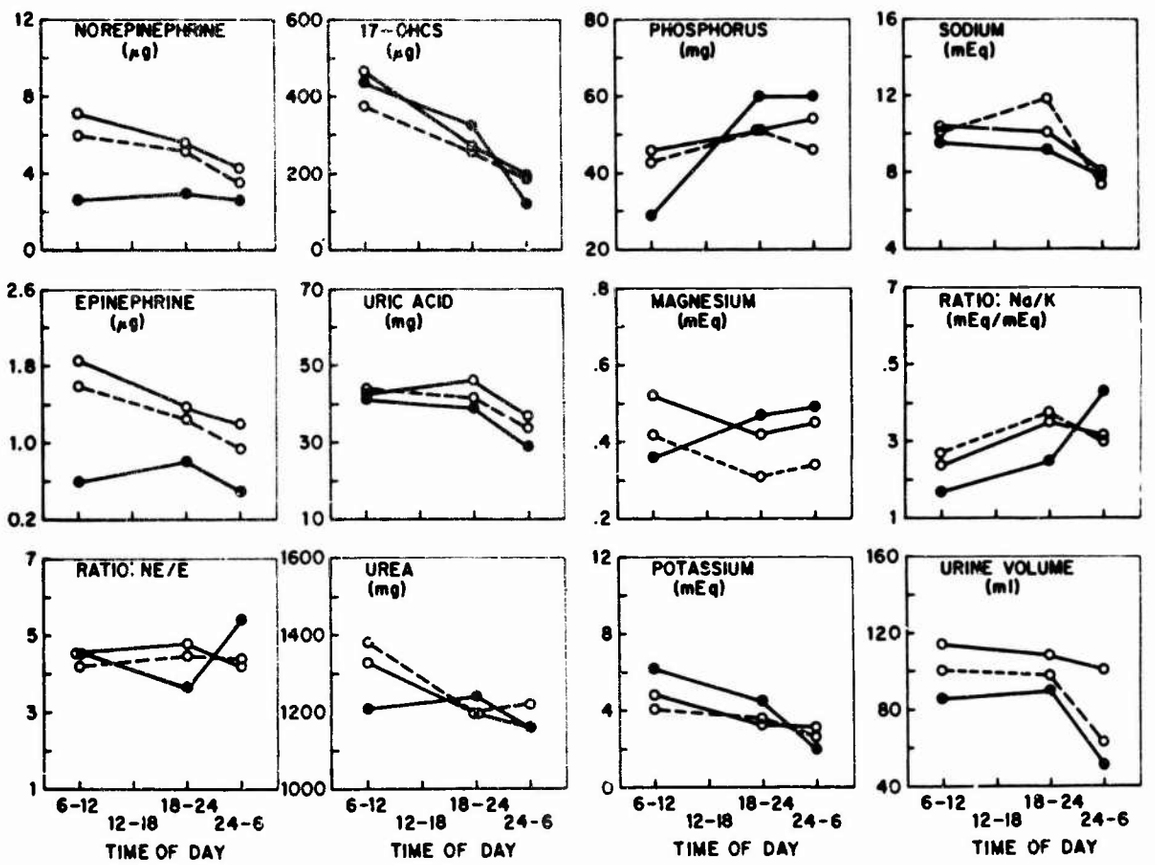


FIGURE 1

Urinary variables in relation to time of day. Filled circles represent laboratory controls; open circles represent flyers. Broken lines represent postflight determinations; unbroken lines represent nonflying circumstances.

progressive movement across all of the earth's time zones did not disrupt circadian rhythms among these particular endocrine-metabolic functions. Also, flight-stress tolerance for the group as a whole seems to have been high.

Seven-week mission

Table VII presents mean values for the representative flyers who were studied during or after the 7-week flying exercise which required overfrequent transcontinental and transoceanic flying. Technical difficulties prevented catecholamine determinations for some of these subjects. Data obtained after transatlantic or transpacific flights were pooled, and comparison was made with control data which were obtained from other flyers 1 week after termination of the exercise. Significant variation was detected for only three of the urinary variables—namely, the NE/E ratio ($P < .001$), potassium ($P < .001$), and the Na/K ratio ($P < .001$). The three NE/E values obtained during the experimental period were all low relative to that obtained in the recovery period, and the latter value exceeded slightly that for the laboratory control. These results are therefore interpreted as indicating mild flight-stress during the experimental period, with overcorrection ("rebound") in the recovery period. On the basis of norepinephrine and epinephrine

TABLE IV

Flight-stress in relation to crew position

Urinary variable*	Year I	Year II				Laboratory control (38)
	Pilots (10)†	Pilots (18)	Flight engineers (10)	Navigators (12)	Loadmasters (7)	
Norepinephrine, μg.	4.77	5.30	4.73	4.68	4.78	2.76
Epinephrine, μg.	1.34	1.49	1.50	0.96	0.83	0.61
Ratio: NE/E	3.6	3.8	3.4	5.0	6.1	4.8
17-OHCS, μg.	243	274	291	269	285	251
Uric acid, mg.	33	41	44	35	38	34
Urea, mg.	1,254	1,257	1,281	1,277	1,288	1,191
Phosphorus, mg.	43	45	52	39	50	52
Magnesium, mEq.	0.55	0.43	0.28	0.34	0.32	0.45
Potassium, mEq.	2.3	3.0	3.9	3.7	3.1	3.7
Sodium, mEq.	8.2	9.5	8.2	11.5	8.1	8.7
Ratio: Na/K	3.8	3.4	2.2	3.4	3.0	3.2
Volume, ml.	78	82	85	101	67	70

*Except where otherwise indicated, each urinary variable is a creatinine-based ratio (quantity/100 mg. creatinine).
†Number in parentheses is number of subjects.

TABLE V

Effects of nighttime C-130E flights over different routes

Urinary variable*	Antarctica–New Zealand Flight		Hawaii–New Zealand Flight		Laboratory control (12)
	Postflight (18)†	Control (18)	Postflight (7)	Control (7)	
Norepinephrine, μg.	3.64	4.30	4.10	3.37	2.64
Epinephrine, μg.	0.94	1.20	1.29	0.90	0.51
Ratio: NE/E	4.4	4.2	3.4	4.5	5.4
17-OHCS, μg.	190	198	253	246	121
Uric acid, mg.	34	37	41	27	29
Urea, mg.	1,223	1,156	1,379	1,171	1,158
Phosphorus, mg.	46	54	63	56	60
Magnesium, mEq.	0.34	0.45	0.48	0.42	0.49
Potassium, mEq.	2.6	3.1	2.8	2.3	2.0
Sodium, mEq.	7.6	8.1	8.5	5.7	7.9
Ratio: Na/K	3.0	3.1	2.9	2.4	4.3
Volume, ml.	63	101	71	73	51

*Except where otherwise indicated, each urinary variable is a creatinine-based ratio (quantity/100 mg. creatinine).
†Number in parentheses is number of subjects.

values, it appears that low-grade sympathoadrenal stimulation occurred during the experimental period; however, the number of subjects was small, and statistical support was not obtained. The catecholamine values in the recovery period are intermediate to the experimental and control values, which suggests incomplete reversal of flight-induced changes. Although the individual catecholamine findings, by themselves, are questionable since they lack statistical support, there is indirect support which comes from the NE/E ratio. Potassium excretion showed sustained depression throughout the experimental period, with prompt reversal to the control level in the recovery period. In turn, the Na/K ratio showed sustained elevation throughout the experimental period, with reversal in the recovery period. Progressive elevation during the experimental period is evident for urea, phosphorus, and magnesium; and each shows what appears to be partial reversal in the recovery period. Such trends might be expected in repetitive stress; however, since statistical support was lacking in the present case, these trends are questionable.

It had been hoped that each of the subjects studied during the experimental period would be available for study during the recovery period; but only 13 were so studied, and catecholamine data were not obtainable in these particular cases. The postflight and recovery data for this special group appear in table VIII. Certain of the above-mentioned trends (which were based upon data for different groups of subjects) were verified by use of this repeatedly studied group of subjects. The flight-induced reduction in potassium excretion, along with the reversal in the recovery period, was clearly demonstrated by this group, as was the elevation (and later reversal) in the Na/K ratio. Urea and phosphorus levations were not demonstrable, but the magnesium elevation appeared and had statistical support. Additionally, a statistically significant flight-induced rise in uric acid excretion was found. This was readily reversed. In the recovery period, this particular group of flyers showed close agreement with the laboratory control group in most respects. Still, the 17-OHCS value tended to be high relative to the laboratory control value which probably indicates incomplete reversal.

Time of day was a factor in this study that could not be standardized. Table IX presents a time-based breakdown of the postflight data, a different group of subjects representing each quarter of the day. As organized, this table brings out effects of sleep deprivation. The afternoon data (1200 to 1800 hours) are considered the basic ones, as they are not complicated by the antecedent factor of sleep deprivation. The data obtained in the evening (1800 to 2400 hours), at night (2400 to 0600 hours), and in the forenoon (0600 to 1200 hours) can be expected to be complicated to an increasingly greater extent by the factor of sleep deprivation. Figure 2 presents the data for the different groups of flyers in the form of composite curves, with time of day as the independent variable. The norepinephrine curves for the flyers and the controls show divergence, as do the epinephrine curves. When expressed as percent of the laboratory control values, the postflight norepinephrine values for afternoon, evening, night, and forenoon amount to 110%, 132%, 168%, and 301%, respectively; while the epinephrine values amount to 123%, 133%, 267%, and 417%. While confirmatory studies will certainly be needed, as the present number of subjects is small, this gradation in postflight catecholamine excretion leads to the tentative conclusion that sympathoadrenal sensitivity to flight is increased by sleep deprivation. As additional evidence of this, the NE/E ratios for the flyers were essentially normal in the afternoon and evening, thereby indicating that flight effects on the two parts of the sympathoadrenal system were slight; but at night and in the forenoon, when sleep deprivation was an added factor, flight blocked the upward shift in the NE/E ratio that appears to be normal for these times of day. Flight also had a blocking action on the diurnal shift in 17-OHCS excretion, preventing the normal nighttime reduction (fig. 2). Phosphorus excretion (fig. 2) for the flyers was essentially normal at all times of day except forenoon, at which time there was upward deviation. This latter difference possibly can be interpreted

TABLE VI

Six-day mission

Urinary variable*	1500 to 2300 hours			1500 to 1900 hours
	Preflight (24)†	Postflight (27)	Control (27)	Laboratory control (26)
17-OHCS, μg.	274	338	281	358
Uric acid, mg.	43	43	43	40
Urea, mg.	1,239	1,160	1,255	1,208
Phosphorus, mg.	59	50	54	54
Magnesium, mEq.	0.64	0.61	0.78	0.39
Potassium, mEq.	4.2	3.6	4.2	4.8
Sodium, mEq.	11.3	9.4	10.6	9.0
Ratio: Na/K	3.1	2.8	2.8	2.2
Volume, ml.	87	78	121	81

*Except where otherwise indicated, each urinary variable is a creatinine-based ratio (quantity/100 mg. creatinine).

†Number in parentheses is number of subjects.

TABLE VII

Seven-week mission

Urinary variable*	Experimental period			Recovery period	Laboratory control (26)
	Weeks 2-4 (15)†	Week 5 (20)	Weeks 6-7 (18)	Week 1 (20)	
Norepinephrine, μg.	[6] 3.31	[13] 4.58	[8] 3.81	3.61	2.94
Epinephrine, μg.	[6] 0.95	[13] 1.33	[8] 1.16	0.91	0.78
Ratio: NE/E	[6] 3.7	[13] 3.4	[8] 3.2	5.5	3.7
17-OHCS, μg.	380	365	364	383	358
Uric acid, mg.	41	42	45	40	40
Urea, mg.	1,186	1,484	1,704	1,231	1,208
Phosphorus, mg.	30	54	65	50	54
Magnesium, mEq.	0.40	0.54	0.70	0.53	0.39
Potassium, mEq.	2.5	2.6	2.6	5.1	4.8
Sodium, mEq.	10.1	11.6	9.8	10.8	9.0
Ratio: Na/K	4.4	5.1	4.3	2.0	2.2
Volume, ml.	78	98	97	93	81

*Except where otherwise indicated, each urinary variable is a creatinine-based ratio (quantity/100 mg. creatinine). When catecholamine data could not be obtained for some of the members of a group, the number of determinations appears in brackets at the left of the group value.

†Number in parentheses is number of subjects.

TABLE VIII

Chronic flight-stress

Urinary variable*	Experimental period (13)†	Recovery period (13)	Laboratory control (38)
17-OHCS, μg.	402 [NS]	372	279
Uric acid, mg.	42 [P < .005]	34	36
Urea, mg.	1,268 [NS]	1,255	1,190
Phosphorus, mg.	34 [NS]	43	51
Magnesium, mEq.	0.80 [P < .05]	0.47	0.43
Potassium, mEq.	2.4 [P < .005]	4.9	4.0
Sodium, mEq.	12.1 [NS]	8.9	8.7
Ratio: Na/K	5.7 [P < .001]	1.8	2.9
Volume, ml.	85 [NS]	67	70

Except where otherwise indicated, each urinary variable is a creatinine-based ratio (quantity/100 mg. creatinine). Notations given in brackets represent findings in analysis of variance.

†Number in parentheses is number of subjects.

TABLE IX

Time of day as a complicating factor in flight-stress appraisal

Urinary variable*	Afternoon		Evening		Night		Forenoon	
	Flyers (23)†	Controls (26)	Flyers (9)	Controls (26)	Flyers (9)	Controls (12)	Flyers (10)	Controls (26)
Norepinephrine, μg.	[13] 3.14	2.85	[5] 3.99	3.03	[3] 4.47	2.64	[4] 8.20	2.72
Epinephrine, μg.	[13] 0.91	0.74	[5] 1.09	0.82	[3] 1.36	0.51	[4] 2.50	0.60
Ratio: NE/E	[13] 3.4	3.8	[5] 3.8	3.7	[3] 3.2	5.4	[4] 2.9	4.6
17-OHCS, μg.	370	390	366	326	365	121	389	439
Uric acid, mg.	41	42	41	39	44	29	48	42
Urea, mg.	1,498	1,179	1,808	1,237	1,171	1,158	1,494	1,211
Phosphorus, mg.	42	47	53	60	56	60	69	29
Magnesium, mEq.	0.46	0.32	0.58	0.47	0.62	0.49	0.73	0.36
Potassium, mEq.	2.6	5.2	2.4	4.5	2.7	2.0	2.9	6.2
Sodium, mEq.	10.5	8.7	12.0	9.2	9.2	7.9	10.5	9.6
Ratio: Na/K	4.6	1.9	5.8	2.5	4.0	4.3	4.2	1.7
Volume, ml.	73	71	136	90	103	51	96	87

*Except where otherwise indicated, each urinary variable is a creatinine-based ratio (quantity/100 mg. creatinine). When catecholamine data could not be obtained for some members of one of the groups, the number of determinations appears in brackets at the left of the group value.

†Number in parentheses is number of subjects.

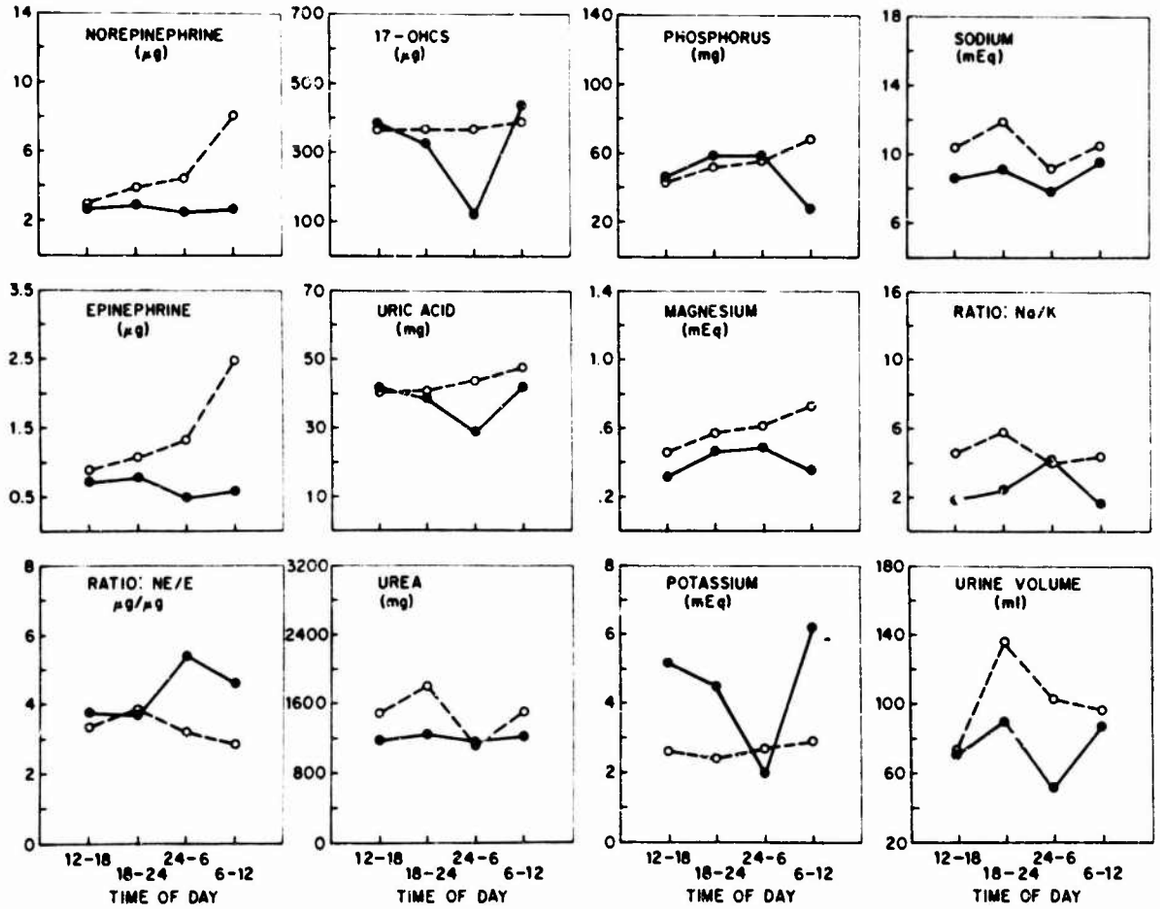


FIGURE 2

Time of day as a complicating factor in flight-stress appraisal. Filled circles represent laboratory controls; open circles represent postflight determinations.

as evidence of a sensitizing action of sleep deprivation. Magnesium curves (fig. 2) for the flyers and nonflyers also show divergence which is limited to the forenoon; this, too, can be considered evidence of increased sensitivity to flight induced by sleep deprivation. While flight effects are evident for K, Na, Na/K, urea, and urine volume (fig. 2), there is little to suggest that sleep deprivation was a contributory factor.

Table X presents urinary data for aircraft mechanics. No evidence of stress was found. In table XI, comparison is made of afternoon values for C-135B commanders, aircraft mechanics, and laboratory staff members. Each value for the mechanics is the average of the three values obtained during the experimental period. In most respects, there is near agreement between comparable values for the mechanics and the laboratory staff members, but the flyers outrank both groups of nonflyers on the basis of norepinephrine, epinephrine, urea, magnesium, and Na/K values. Their low potassium value also differentiates them from the nonflyers. These data suggest that the physiologic "cost" of flying exceeds slightly the "costs" in these other occupations.

IV. DISCUSSION

Schreuder (12), in a recent review of the literature on medical aspects of flight fatigue

TABLE X

Urinary data for aircraft maintenance personnel

Urinary variable*	Experimental period			Control period (22)	Laboratory control (26)
	Week 1 (22)†	Week 3 (22)	Week 6 (22)		
Norepinephrine, μg.	2.29	2.88	2.53	2.08	2.85
Epinephrine, μg.	0.68	0.89	0.70	0.59	0.74
Ratio: NE/E	3.6	3.5	4.0	3.7	3.8
17-OHCS, μg.	334	332	274	336	390
Uric acid, mg.	35	38	35	32	42
Urea, mg.	1,182	1,194	1,043	1,198	1,179
Phosphorus, mg.	51	53	50	57	47
Magnesium, mEq.	0.27	0.34	0.40	0.37	0.32
Potassium, mEq.	4.8	4.8	4.4	4.9	5.2
Sodium, mEq.	12.3	11.1	10.2	11.8	8.7
Ratio: Na/K	2.8	2.6	2.5	2.5	1.9
Volume, ml.	70	81	68	79	71

*Except where otherwise indicated, each urinary variable is a creatinine-based ratio (quantity/100 mg. creatinine).

†Number in parentheses is number of subjects.

TABLE

Comparison of flyers and nonflyers (afternoon data)

Urinary variable*	Flying personnel (postflight) (23)†	Aircraft maintenance personnel (22)	Laboratory personnel (26)
Norepinephrine, μg.	[13] 3.14	2.56	2.85
Epinephrine, μg.	[13] 0.91	0.82	0.74
Ratio: NE/E	[13] 3.4	3.7	3.8
17-OHCS, μg.	370	313	390
Uric acid, mg.	41	36	42
Urea, mg.	1,498	1,140	1,179
Phosphorus, mg.	42	51	47
Magnesium, mEq.	0.46	0.34	0.32
Potassium, mEq.	2.6	4.7	5.2
Sodium, mEq.	10.5	11.2	8.7
Ratio: Na/K	4.6	2.6	1.9
Volume, ml.	78	73	71

*Except where otherwise indicated, each urinary variable is a creatinine-based ratio (quantity/100 mg. creatinine). When catecholamine data could not be obtained for some of the members of a group, the number of determinations appears in brackets at the left of the group value.

†Number in parentheses is number of subjects.

and stress, discussed at length the applicability of the General Adaptation Syndrome concept (13) and emphasized the need for additional studies of endocrine-metabolic responses to flight. The USAF School of Aerospace Medicine has had a long-standing interest in the phenomenon of flight-stress and its quantification and has participated in a series of flight studies (2-5, 7, 8), the purpose of which was to ascertain, under a wide variety of circumstances, the relative importance of factors that are currently thought to contribute either directly or indirectly to the endocrine-metabolic reactions. The present studies add to the variety of the flying circumstances and provide additional information on time and intensity relationships.

Certain of the present findings merit additional comment. Particularly important is the finding that the flight effects tended to be few in number and low in magnitude. As a contrast, pilots who flew transoceanic flights in single-place aircraft (F-100 or F-104) showed numerous flight-related changes, and the magnitude of each change was relatively high (8). The present results suggest either that these particular flyers were physiologically resistant to flight factors or that these flying circumstances were not very stressful. While there were individuals who showed responses of large magnitude, the aggregate response in each case suggested only low-grade stress. The sympathoadrenal responses to flight appeared consistently, but adrenocortical and metabolic responses were not regular in occurrence, nor were they of large magnitude when they were seen. This finding of low sensitivity to flight among the latter functions probably indicates a state of adaptation in these flyers. It is well known that stressors, when first acting on an individual, induce widespread endocrine-metabolic disturbance, and the magnitudes of the adrenocortical and metabolic responses then tend to be relatively large. When there are repeated encounters with a given stressor, the magnitudes of these responses diminish gradually, and only by increasing stressor intensity or by adding secondary factors is it again possible to elicit responses of large magnitude at these particular levels of function. The finding that the secondary factors of crew position and sleep deprivation can act as sensitizers is noteworthy. Also noteworthy is the finding that, with flight circumstances standardized, or essentially so, different groups show similar reactions. With further study, and with some refinement of technic, it may be possible to establish, on an individual basis, flight-stress tolerance ratings. The desirability and usefulness of stress-tolerance ratings remain to be settled. It would also seem worthwhile to ascertain the rate at which flight-stress tolerance can be developed or lost and to devise means for either accelerating or augmenting gains in tolerance.

Also of interest is the finding that endocrine-metabolic effects of flight at times are not readily reversible. This finding may have practical value, for it shows that control data for flyers often may be faulty because of inadequate attention to antecedent circumstances. Additional research is needed in order to ascertain the recovery rates under a variety of flying circumstances, with emphasis on the influence of various factors (acting singly, or in combination) such as crew position, age, amount of flying experience, flight frequency and duration, type of aircraft, and unusual events.

The matter of sleep deprivation and the possibility that it acts as a sensitizing agent toward flight-stress deserves brief comment. Hasselman et al. (6) found unusually high daytime excretion of catecholamines in normal men after a sleepless night; and sleep deprivation was also shown to be a factor capable of altering the sympathoadrenal response to a second factor of an entirely different nature, that of high ambient temperature. In contrast to this, sleep deprivation seems to reduce adrenocortical responsiveness. Murawski and Crabbé (9) demonstrated slightly subnormal daytime 17-OHCS excretion in human subjects after sleep loss, and there were associated changes in amplitude and shape of the diurnal curve for plasma 17-OHCS. The present forenoon 17-OHCS data for 17 sleep-deprived flyers of C-130E aircraft (table III) also suggest mild adrenocortical depression (the postflight and control values were 382 and 472 μg., respectively). Similarly, the forenoon 17-OHCS data

for the 10 sleep-deprived flyers of C-135B aircraft (table IX) indicate depression (the post-flight and control values were 389 and 439 μg., respectively). As a contrasting finding, Kramer et al. (7) reported a statistically significant increase in 17-OHCS excretion for crewmembers of F-4C aircraft who flew 18-hour missions which started in the evening (2300 hours). As a further contrast, the F-4C flyers showed no signs of sympathoadrenal stimulation. Prophylactic measures employed by these particular flyers evidently offset endocrine-metabolic effects of sleep deprivation. These men used secobarbital 12 hours before the start of the flight in order to obtain sleep in advance, and they used dextroamphetamine at various times during the flight to prevent performance decrement.

The low potassium excretion observed in the 7-week study is a finding of importance. According to Selye (13), hyperkaluria and hypokaluria typify the alarm reaction and the stage of resistance, respectively. With hypokaluria as the criterion, we conclude that the C-135B flyers, as a group, reached the stage of resistance at an early time in the experimental period. Although the flight-induced hypokaluria is not currently explainable, it appears to represent catecholamine-corticosteroid interplay. While this is only speculation, it is founded on well-known endocrine actions. Smythe et al. (14) showed that catecholamines depress the urinary excretion of potassium in normal human subjects, doing so by augmenting renal tubular reabsorption. It is well known that 17-OHCS have the opposite effect on potassium excretion (13). Relatively normal 17-OHCS excretion was demonstrated for the C-135B flyers; but there was significant variation in the NE/E ratio, and the separate catecholamines on the average exceeded laboratory control levels. It therefore seems likely that the low potassium excretion relates to the flight-induced sympathoadrenal stimulation. Without a concomitant change in adrenocortical activity, the sympathoadrenal system apparently becomes the primary mechanism of control for potassium excretion. Further investigation is needed to settle this question.

REFERENCES

1. Feller, R. P. Modification of the trihydroxyindole method for the estimation of epinephrine and norepinephrine in urine. SAM Report 60-71, Aug. 1960.

2. Hale, H. B., J. C. Duffy, J. P. Ellis, Jr., and E. W. Williams. Flying stress in relation to flying proficiency. Aerospace Med. 36:112-116 (1965).

3. Hale, H. B., J. P. Ellis, Jr., and C. H. Kratochvil. Effects of piloting supersonic aircraft on plasma corticosteroids and bicarbonate. J. Appl. Physiol. 14:629-631 (1959).

4. Hale, H. B., J. P. Ellis, Jr., and E. W. Williams. Endocrine and metabolic changes during a 12-hour simulated flight. Aerospace Med. 36:717-719 (1965).

5. Hale, H. B., C. H. Kratochvil, and J. P. Ellis, Jr. Plasma corticosteroid levels in aircrewmen after long flights. J. Clin. Endocr. 18:1440-1443 (1958).

6. Hasselman, M., G. Schaff, and B. Metz. Influences respectives du travail, de la température ambiante et de la privation de sommeil sur l'excrétion urinaire de catécholamines chez l'homme normal. C. R. Soc. Biol. (Paris) 154: 197-201 (1960).

7. Kramer, E. F., H. B. Hale, and E. W. Williams. Physiological effects of an 18-hour flight in F-4C aircraft. Aerospace Med. 37:1095-1098 (1966).

8. Marchbanks, V. H., Jr., H. B. Hale, and J. P. Ellis, Jr. Stress responses of pilots flying 6-hour overwater missions in F-100 and F-104 aircraft. Aerospace Med. 34:15-18 (1963).

9. Murawski, B. J., and J. Crabbé. Effect of sleep deprivation on plasma 17-hydroxycorticosterolds. J. Appl. Physiol. 15:280-282 (1960).

10. Reddy, W. J. Modification of the Reddy-Jenkins-Thorn method for estimation of 17-hydroxycorticosteroids in urine. Metabolism 3:489-492 (1954).

11. Schachter, D. Fluorometric estimation of magnesium with 8-hydroxy-5-quinoline-sulfonate. J. Lab. Clin. Med. 58:495-498 (1961).

12. Schreuder, O. B. Medical aspects of aircraft pilot fatigue with special reference to the commercial jet pilot. Aerospace Med. 37(4,II):1-44 (1966).

13. Selye, H. The physiology and pathology of exposure to stress. Montreal: Acta, 1950.

14. Smythe, C. M., J. F. Nickel, and S. E. Bradley. The effect of epinephrine (USP), l-epinephrine, and l-norepinephrine on glomerular filtration rate, renal plasma flow, and the urinary excretion of sodium, potassium, and water in normal man. J. Clin. Invest. 31:499-506 (1952).

Unclassified
Security Classification

DOCUMENT CONTROL DATA - R & D

(Security classification of title, body of abstract and indexing annotation must be entered when the overall report is classified)

1. ORIGINATING ACTIVITY *(Corporate author)*
USAF School of Aerospace Medicine
Aerospace Medical Division (AFSC)
Brooks Air Force Base, Texas

2a. REPORT SECURITY CLASSIFICATION
Unclassified

2b. GROUP

3. REPORT TITLE
ENDOCRINE-METABOLIC EFFECTS OF UNUSUALLY LONG OR FREQUENT FLYING MISSIONS IN C-130E OR C-135B AIRCRAFT

4. DESCRIPTIVE NOTES *(Type of report and inclusive dates)*
Final Nov. 1964 - Dec. 1967

5. AUTHOR(S) *(First name, middle initial, last name)*
Henry B. Hale
Clarence A. Anderson, Captain, USAF, MC
Edgar W. Williams
Emanuel Tanne, Captain, USAF, MC

6. REPORT DATE	7a. TOTAL NO. OF PAGES	7b. NO. OF REFS
March 1968	16	14

8a. CONTRACT OR GRANT NO.	9a. ORIGINATOR'S REPORT NUMBER(S)
b. PROJECT NO.	SAM-TR-68-24
c. Task No. 775801	9b. OTHER REPORT NO(S) *(Any other numbers that may be assigned this report)*
d.	

10. DISTRIBUTION STATEMENT
This document has been approved for public release and sale; its distribution is unlimited.

11. SUPPLEMENTARY NOTES	12. SPONSORING MILITARY ACTIVITY
	USAF School of Aerospace Medicine Aerospace Medical Division (AFSC) Brooks Air Force Base, Texas

13. ABSTRACT

Flight-stress appraisal was made by means of a battery of urinary determinations (epinephrine, norepinephrine, 17-OHCS, urea, uric acid, phosphorus, magnesium, sodium, and potassium) for flyers who participated in (a) 20-hour missions in C-130E aircraft (flights from New Zealand to Antarctica, and back), (b) 6-day missions in C-135B aircraft (earth-circling missions), or (c) 7-week missions in C-135B aircraft (over-frequent transoceanic and transcontinental flying). The adrenal medulla (as judged by urinary epinephrine) consistently showed flight-sensitivity, but other endocrine-metabolic functions varied in ways indicative of adaptation. With flight circumstances standardized (particularly with respect to time of day), flight effects tended to be reproducible. With crew rest limited to 2 days, recovery from flight-stress tended to be incomplete. Sleep deprivation and crew position were shown to be factors which modify flight-stress reactions. Eastbound and westbound earth-circling missions did not induce different degress of flight-stress, as judged by these endocrine-metabolic indices.

DD FORM 1 NOV 65 1473

Unclassified
Security Classification

14 KEY WORDS	LINK A		LINK B		LINK C	
	ROLE	WT	ROLE	WT	ROLE	WT
Physiology						
Flight stress						
Urinary catecholamines						
17-Hydroxycorticosteroids						
Urinary metabolites						