AM 65-28

PHASE SHIFTS OF THE HUMAN CIRCADIAN SYSTEM AND PERFORMANCE DEFICIT DURING THE PERIODS OF TRANSITION:

I. East-West Flight

G. T. Hauty, Ph. D.

T. Adams, Ph. D.

Approved by

J. Robert Dille, M.D.
Chief, Civil Aeromedical Institute

Released by

P. V. Siegel, M.D.
Federal Air Surgeon

December 1965

FEDERAL AVIATION AGENCY

Office of Aviation Medicine

Qualified requestors may obtain Aviation Medical Reports from Defense Documentation Center. The general public may purchase from Clearinghouse for Federal Scientific and Technical Information, U.S. Dept. of Commerce, Springfield, Va. 22151

PHASE SHIFTS OF THE HUMAN CIRCADIAN SYSTEM AND PERFORMANCE DEFICIT DURING THE PERIODS OF TRANSITION:

I. East-West Flight

I. Introduction.

Since rapid translocation through many time zones involves disruption of circadian periodicity with pronounced subjective effects, it is understandable that intercontinental air carrier crews would claim these effects to be partially responsible for the production of fatigue. Further, such a claim is enhanced by the possibility that crew scheduling may be at variance with the time lag for readjusting biological processes because present schedules are not based on objective determinations of the effects concerned or derived from relevant scientific information. Such determinations have yet to be made, and sufficient relevant information is not available.

Most of the experimental studies of human periodicity [3, 10, 12, 13] have been prompted by etiological considerations necessitating environmental conditions and controls that preclude fruitful extrapolation. Studies that have dealt directly with the problem are few.[7–9, 16] With one exception,[5] the respective subject-population size was small, and, for the most part, only a single function rather than a spectrum of biological activities was assessed.

Accordingly, a series of intercontinental flights was undertaken for the purpose of obtaining information pertinent to those basic questions most obviously in need of initial and definitive answer:

(1) What is the extent of time lag for biological phase shifts under these circumstances?

(2) To what extent, if any, is proficiency adversely affected during the period of transition?

(3) What is the extent and nature of differences manifested during the primary and the back shifts and their respective transitional periods?

(4) To what extent do individuals differ in lag time and adverse effects upon proficiency?

The first flight, a jet flight from Oklahoma City to Tokyo and return, was primarily a feasibility study of the problems of experimental control, logistics, and tolerances of volunteer subjects. With the obtained information,[11] three subsequent flights were planned and completed: (1) East-West; (2) a West-East round-trip jet flight that permitted a comparative analysis of bidirectional time-zone displacement effects; and (3) a North-South jet flight that, as a "control," provided an appraisal of those effects solely attributable to prolonged flight.

Subjects were selected from a group whose daily habits of work and sleep were representative of the general, adult, male population because of the need for a reference against which to compare findings obtained from intercontinental air carrier crews.

Owing to the large volume of data, these flights will be reported separately and in the order of their occurrence. First to be reported is the East-West flight, which originated in Oklahoma City and consisted of jet flight to and from Manila. Time of departure was 1800 hours CST, total time in transit 23-½ hours, time of arrival in Manila 0730 hours local time, and time displacement was 10 hours.

II. Method.

A. *Schedule of Assessment.*—Periodic biomedical assessments were made on *alternate* days during the week immediately prior to flight, during a period of layover at Manila, and during the week following return to Oklahoma City. This schedule provided a reference of biological time set to the environment of origin (Oklahoma City) and periods of transition for the "primary" shift (Oklahoma City-Manila) and for the "back" shift (Manila-Oklahoma City).

Biomedical assessments were repeated at 0700, 1100, 1500, 1900, and 2300 hours (local time) on each day of assessment. During each of these five periods of assessment, several different psychological functions were sequentially assessed by highly standardized procedures. Simultaneously, assessment was also made of several different physiological functions. Time required for such a period was approximately 25 minutes.

The decision to test on alternate days was based on the results of the feasibility flight (Tokyo), which indicated that successive days of assessment placed a greater than expected imposition upon the subjects and may have contributed to their self-reported state of fatigue. The duration of the testing period in Manila (8 days) was also derived from the feasibility flight, which revealed the period of time required for the shift of phase to Tokyo time.

B. *Assessments.*—The biomedical assessments to be reported include:

1. *Rectal Temperature.* Internal body temperature was measured by a portable, indicating bridge circuit, calibrated to a thermistor rectal probe. In order to reduce the indicated artifacts of rectal-temperature recording,[14] the rectal probe was inserted to a depth of 10-cm, worn continuously throughout each assessment day, and removed only for bathing or evacuation. During transitional overseas movements, the rectal probe was worn from 0600 hours on the day of departure through 5 successive days, and subsequently for 24-hour periods on alternate days. During the waking portion of the day, the subject read and recorded his own temperature to the nearest 0.1°C at 30-minute intervals; for the remainder of the day, a technician recorded the sleeping subject's temperature at the same interval. No untoward consequences, other than minor inconvenience, were reported by the subjects as a consequence of the prolonged periods of rectal-probe insertion.

2. *Evaporative Water Loss.* The method for quantitatively measuring skin-surface evaporative water loss has been described earlier.[1, 2] For each assessment period, a small plastic capsule, sampling from a 1-sq cm skin area, was sealed to the skin at the center of the left palm. Measurements of evaporative water loss from this area were made continuously throughout each assessment, evaluating both steady-state "basal" levels during rest before and after each assessment period and increased evaporative rates during identified assessment increments. These data were examined to provide measurements of "basal" evaporative water loss, increases in instantaneous rates related to matched assessments, and the total amount of water evaporated during the entire assessment period and its individual subcomponents.

3. *Heart and Respiratory Rates.* A lightweight, plastic and elastic chest strap was improvised to house three silver electrodes for heart-rate measurements and a mercury-in-rubber strain gage to monitor respiratory rate as a function of changes in chest circumference. The chest strap was fitted to the subject at the beginning of each assessment period and removed at the end of the period. Heart rates were recorded from a standard indicating cardiotachometer (Phipps-Bird, Model 70-781) at 30-second intervals. Respiratory movements were recorded through an appropriate matching bridge (Model 270 Plethysmograph, Parks Elect. Lab.) on a millivolt strip-chart recorder.

4. *Reaction Time.* The speed of manual response to a variety of stimuli and stimulus conditions was measured by means of a Lafayette Multi-Choice Reaction Timer modified to preclude secondary cues. Responses were elicited in order by three successive presentations of a single auditory stimulus, three successive presentations of a single visual stimulus, six successive and randomly determined presentations of one of three possible visual stimuli, and finally by one presentation of the single auditory stimulus. Intervals of presentation were irregular.

5. *Decision Time.* This was obtained for each assessment period by subtracting the mean time of responding to the three presentations of the single visual stimulus from the mean time of responding with the correct response to the six presentations of one of the three different visual stimuli. This value is taken to represent the average time required to "decide" which of the three possible responses was the correct response to be made.

6. *Critical Flicker-Fusion.* Three ascending and three alternating descending thresholds were determined by a Lafayette Flicker-Fusion apparatus. In indicating the highest rate at which this type of input can be adequately processed, these thresholds are generally considered representative of the state of efficiency of cerebral function, and, when used as an index of fatigue, an inverse relationship between flicker-fusion threshold and hours of work is sometimes reported.[4]

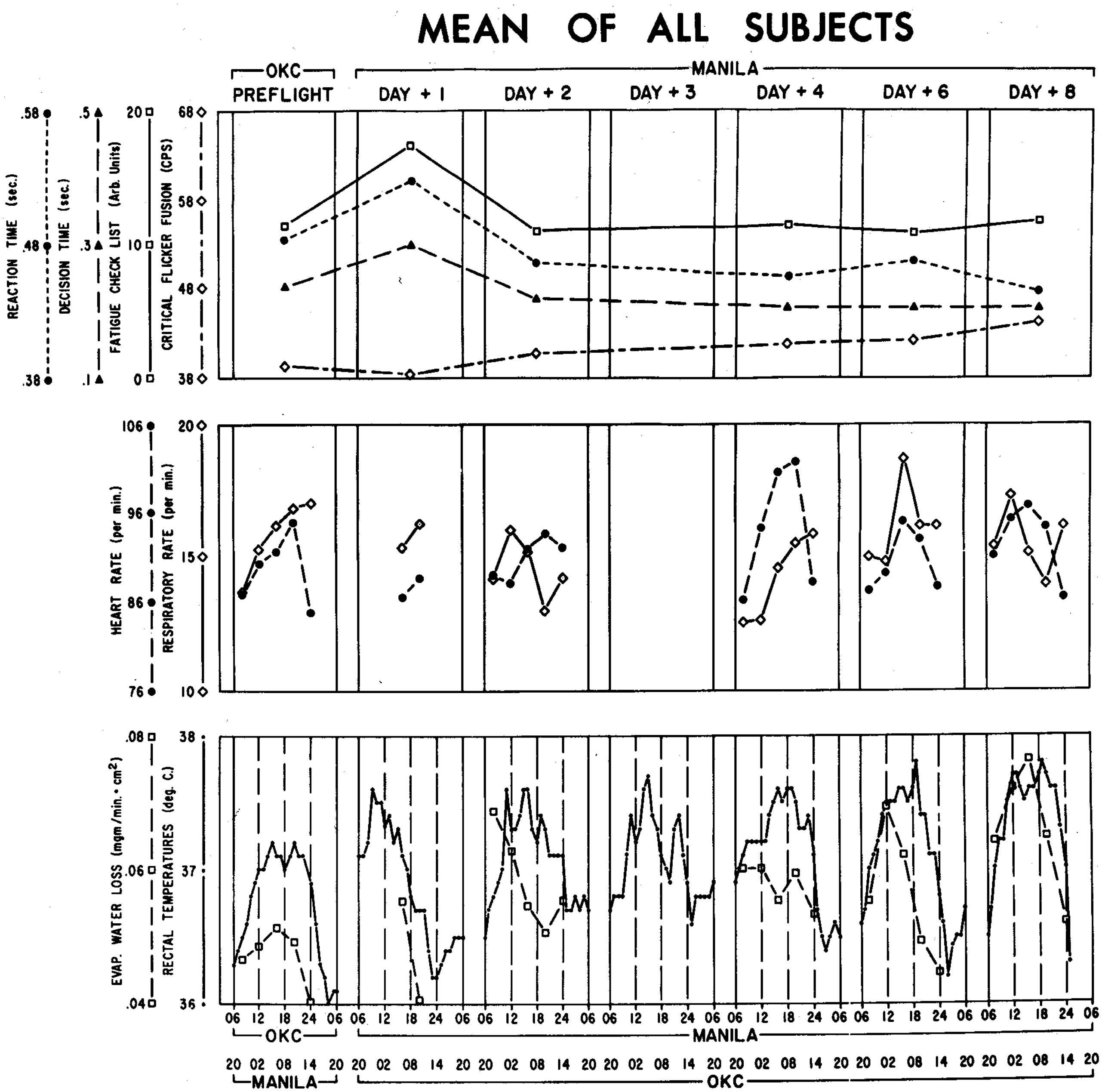

FIGURE 1. Mean plottings of data obtained in Oklahoma City (preflight) and in Manila (layover).

7. *Subjective Fatigue.* The level of subjective fatigue was measured by means of checklists that were developed by the scale discrimination method and that were shown to reflect significantly the effects of perceptual-motor work and, also, the effects of pharmacological treatment.[15]

C. *Subjects.*—Four healthy, adult, male volunteers were drawn from the professional and technical staffs of the Civil Aeromedical Research Institute. During all periods of assessment, preflight, overseas, and post-return flight, the subjects were quartered in wards permitting supervision of activity. Finally, the subjects were instructed to maintain their daily living habits in accordance with the local time of the overseas destination immediately following arrival.

III. Results.

A. *Primary Shift.*—The results obtained during the preflight (Oklahoma City) and postflight

(Manila) days of assessment are given by Figure 1.
Here, for each assessed function, the plotted values are the means of the four subjects for each hour for rectal temperature; for each assessment period for palmar evaporative water loss, heart rate, and respiratory rate; and for each day of assessment for the psychological functions. The values plotted for preflight represent the pooled means of the four subjects for the last 2 days of preflight assessment, which were observed as being least contaminated by novelty or unfamiliarity.

1. *Rectal Temperature.* Examination of the preflight curve of rectal temperature reveals the periodicity and amplitude of stored heat typically obtained under normal circumstances; i.e., following awakening, temperature is seen to increase steadily, plateau between 1400 and 2000 hours, then decline steadily to the beginning of the next biological day. In contrast, the curve of rectal temperatures obtained the first day in Manila (Day + 1) is distinctly out of phase with the local time of Manila and with the time of Oklahoma City. It is not until Day + 4 that the phase shift appears to have been completed. This gradual shifting of phase is shown more clearly in Figure 2, in which the rectal-temperature means for each day are plotted with separate ordinates on a common abscissa (local time).

Another major alteration in the daily curves of internal body temperature is shown in Figure 1. In Oklahoma City, the upper mean level of internal thermal stability is seen to be approximately 37.1°C. In Manila, a progressive increase in mean level occurs, resulting in an elevation of thermal stability to a level of approximately 37.8°C by Day + 8.

2. *Palmar Evaporative Water Loss.* Plotted with the temperature curves in Figure 1 are the mean values for resting palmar evaporative water loss obtained during each period of assessment. As is revealed by the preflight plottings, this function also appears to manifest circadian periodicity with a phase closely associated with that of rectal temperature. This association, however, is markedly affected by the time displacement incurred. The shift in phase of internal temperature appears to have been completed on Day + 4; the complete shift of phase of palmar evaporative water loss does not occur until Day + 8. A clearer representation of this phase shift is given

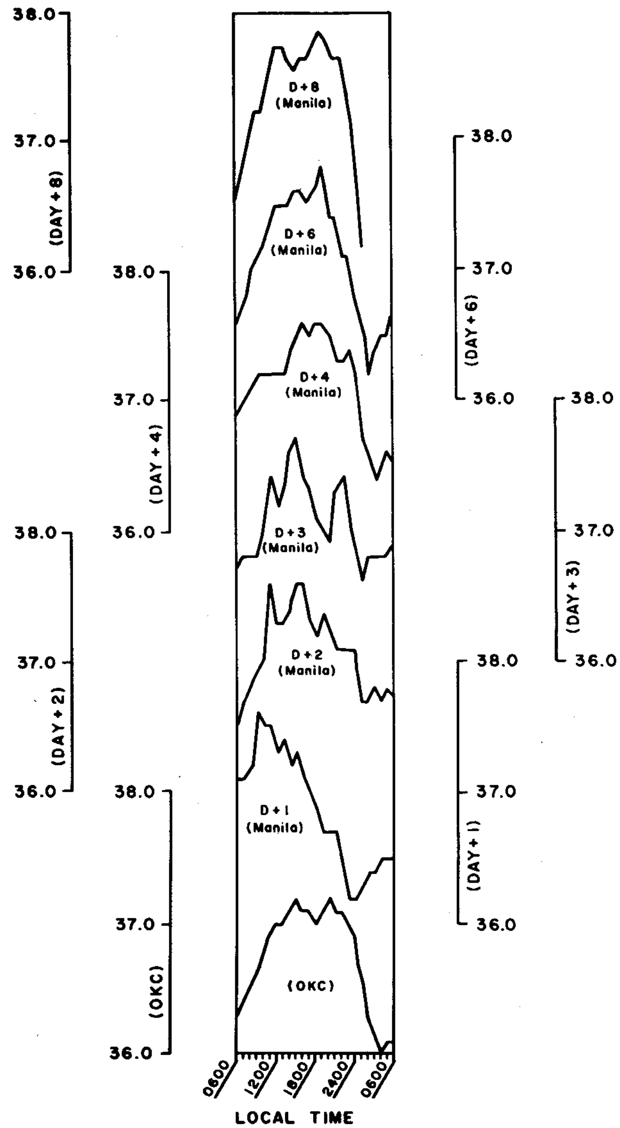

FIGURE 2. Mean plottings of rectal temperature during preflight (Oklahoma City) and during layover period in Manila.

by Figure 3. Also revealed by Figures 1 and 3 is the gradual elevation of palmar evaporative water loss from a mean plateau value of 0.048 mg/min sq cm in Oklahoma City to 0.070 mg/min sq cm on Day + 8 in Manila.

Because of the fatigued state of the subjects due to their arrival time and customs delay, assessments could only be made at 1500 and 1900 hours but not at 2300 hours.

3. *Heart Rate.* Circadian periodicity is also revealed by the preflight values plotted for heart rate (Figure 1) and, as for palmar evaporative water loss, its phase is seen to be closely associated with that of internal temperature. Unlike

palmar evaporative water loss, however, its time lag is about that of rectal temperature.

4. *Respiratory Rate.* In contrast to the other physiological functions, respiratory rate does not show a periodicity of well-defined and consistent nature.

5. *Reaction Time.* The reaction-time values shown in Figure 1 represent the average speed of appropriate manual response to a variety of stimuli and stimulus conditions throughout each day of assessment. Using the preflight value as a basis for comparison, reaction time is seen to increase substantially (i.e., become slower) during Day + 1. On Day + 2, reaction time decreases (improves in speed) to a level slightly below that attained during preflight. Analyses of the variance attributable to replicated days of assessment reveal the increment of reaction time on Day + 1 to be significant at the $>0.05<0.10$ level of confidence. The gradual improvement of reaction time shown during the subsequent days in Manila may be attributed largely to "practice effect," which was not completely eliminated by the considerable amount of practice given the subjects prior to the last 2 preflight days of assessment.

6. *Decision Time.* The values plotted for decision time in Figure 1 represent the daily mean

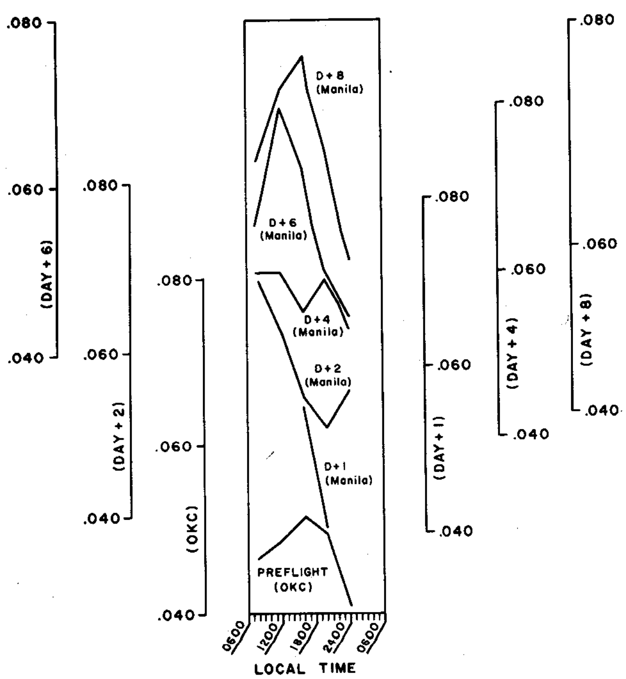

FIGURE 3. Mean plottings of palmar evaporative water loss during preflight (Oklahoma City) and during layover period in Manila.

speed of decision as this has been defined. As in the case of reaction time, decision time increases (becomes slower) on Day + 1, returns toward the preflight level on Day + 2, and remains about this level for the remaining days of assessment in Manila. In using the above-mentioned model for analysis of variance, the increase in decision time noted for Day + 1 was found to be highly significant ($P = 0.001$).

7. *Subjective Fatigue.* The index of subjective fatigue was scaled from "extremely fatigued" to "extremely alert"; consequently, the higher the daily mean values seen plotted in Figure 1, the more fatigued the subjects felt themselves to be. From the curves of psychological function seen thus far, subjective fatigue would be expected to be greater on Day + 1; this is borne out. On Day + 2, the mean value has returned to preflight level and remains about this level during the subsequent days in Manila. This increment observed for Day + 1 was also found to be statistically significant ($P = 0.01$).

8. *Critical Flicker-Fusion.* It was expected that the curve of mean flicker-fusion thresholds seen in Figure 1 would agree with the other curves of psychological function. Had this occurred, a substantial decrease would have been evidenced on Day + 1. Since this is not in evidence, it must be concluded that efficiency of cerebral function was either improperly assessed or negligibly affected.

B. *Back Shift.*—Due to commercial carrier schedules, the return flight to Oklahoma City could not be made under comparable conditions of transit. Whereas the flight to Manila was made in a total of 23-½ hours with no more than 2-½ hours for any layover, the return flight required a total of 34 hours and an overnight layover in Los Angeles. Arrival time in Los Angeles was 2330 hours CST, departure was 1100 hours the following day, and arrival in Oklahoma City was 1330 hours. The first day of postflight assessment followed the day of arrival in Oklahoma City. This difference must be kept in mind when comparing the primary and back shifts.

The results are presented by Figure 4. Here, the basis for determining the effects of time displacement occasioned by the flight back to Oklahoma City consists of the values obtained during the last assessment day in Manila.

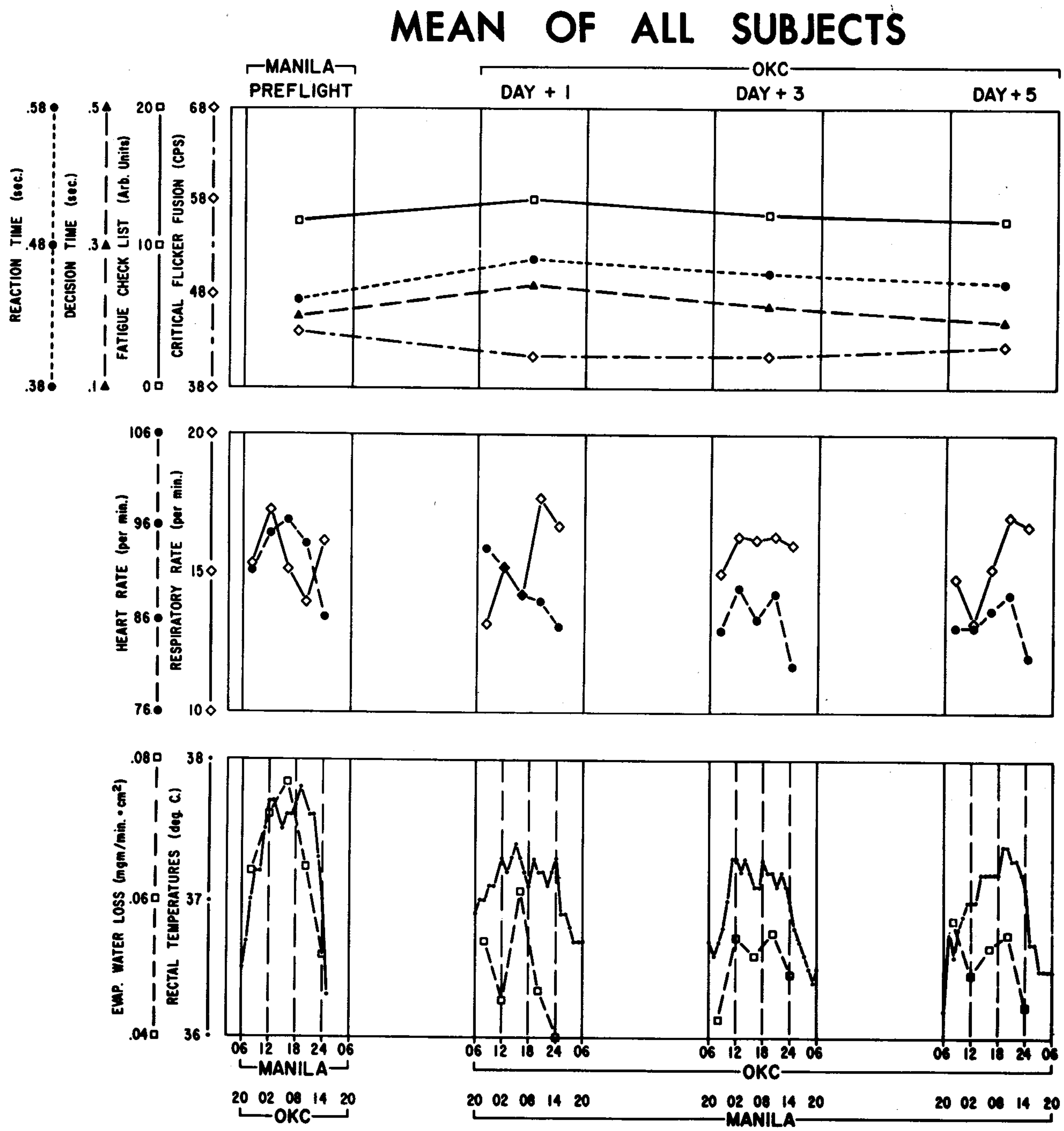

FIGURE 4. Mean plottings of data obtained in Manila (preflight) and in Oklahoma City (return flight).

1. *Physiological Functions.* In contrast to the time lag for the primary shift, the lag in time during the back shift would seem to be shorter. Both rectal temperature and palmar evaporative water loss curves show a complete shift in phase to Oklahoma City time on Day + 1. The mean levels of internal temperature and of palmar evaporative water loss have fallen to the Oklahoma City preflight level on Day + 1 and remain at this baseline level throughout the remaining days of assessment. Figures 5 and 6 exhibit these findings more clearly.

An exception, perhaps, to the "immediate" back shift may be that of heart rate. Apparently, the phase shift of this function is not complete until Day + 3.

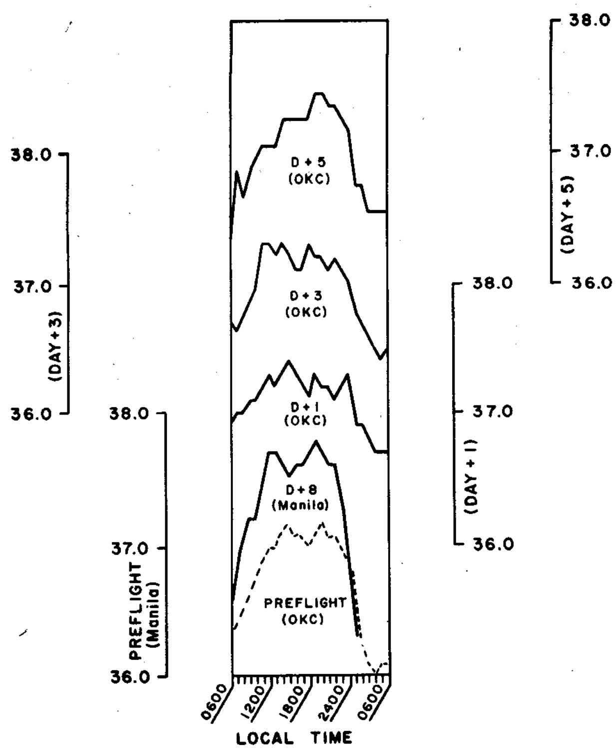

FIGURE 5. Mean plottings of rectal temperature during preflight (Manila – Day + 8) and following return to Oklahoma City.

2. *Psychological Functions.* In general support of the foregoing are the curves of reaction time, decision time, and subjective fatigue plotted in Figure 4. Some deficit does occur on Day + 1 but to a much less extent than on Day + 1 in Manila.

IV. Discussion.

Despite differences in extent of time displacement, flight duration, arrival time, test conditions, and sampling, the data reported here are in agreement with data obtained in the previous flight[11] which, while primarily a feasibility study, did yield information pertinent to the questions underlying this research.

With respect to the first such question then (namely, biological lag time of phase shifting), it would appear that statements or assumptions of biological adjustment to time displacement must be qualified by restricting adjustment in this instance to the specific function or functions assessed. As has been seen, the time lag of the primary phase shift of rectal temperature was approximately 4 days and for palmar evaporative water loss was approximately twice as long. Other functions may be characterized by even longer time lags.

The progressive daily mean rise in rectal temperature and palmar evaporative water loss observed during the period of assessment in Manila cannot be attributed directly to any differences in thermostasis due to acute shifts in environmental thermal exposure. Even if it were to be argued that the difference between the mean level noted in Oklahoma City (preflight) and that evidenced on Day + 8 in Manila (0.7°C) reflects the dead-zone range of biothermal control, such an elevation of internal temperature would be expected to occur within a few hours following arrival in Manila. Moreover, these data were collected from subjects resting under conditions of controlled ambient temperatures for periods more than long enough to permit dissipation of any stored heat due to thermal loading by prior exercise or heat exposure. This elevation cannot be attributed to any degree of thermal-stress acclimatization since the measured adjustment period was too short, and only a mild degree of thermal stress was encountered. Further, these temperatures were taken under conditions of rest

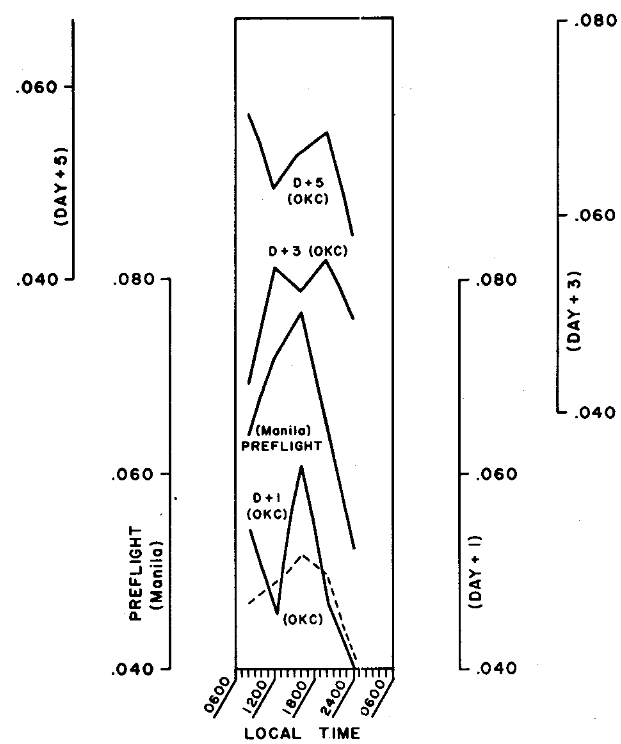

FIGURE 6. Mean plottings of palmar evaporative water loss during preflight (Manila – Day + 8) and following return to Oklahoma City.

at neutral ambient temperatures unlike those under which acclimatization indexes become evident.

In contrast to the time lags seen for the physiological functions, the duration of psychological deficit was exceedingly short. In fact, this deficit, which was occasioned presumably by the joint effects of time displacement and prolonged flight, appeared to have been eliminated by the first night of sleep in Manila. This elimination was also found in the Tokyo flight. The short duration of this performance deficit was surprising because a higher degree of relationship was expected between duration of deficit and the time required for the physiological functions to shift to Manila time. The basis for this expectation consisted of the comments volunteered by the subjects, indicating that "adjustment" to Manila time as subjectively perceived by the subjects was closely related to the course of physiological adjustment. Such comments pertained to sleep, eating, and other similar habitual daily regimens. And, at times, the remark would be made that as soon as they "got on schedule," they would be able to perform better on the psychological tasks. The fact that the duration of performance deficit is also unrelated to subjectively perceived "adjustment" serves to enhance significantly the practical implication of this finding. Finally, it should be made explicit that the duration and extent of performance deficit demonstrated might well be a function of the simplicity of the functions assessed. Had the assessment schedule permitted the time required for the testing of much more complex functions such as higher-order decision making, extent and duration of deficit might have been greater.

The results of the return flight to Oklahoma City, which agree with earlier studies [9] and with the results of the Tokyo flight, [11] are also of practical importance. Evidence that would serve to explain why the return to the environment of origin appears to impose a much less severe requirement upon the adjustive processes involved is not available. Based upon speculation that has been advanced,[6] however, it could be argued that, within the period of time at Manila, certain biological functions may not have completed the shift of phase. For others, possibly, phase shifting might not have begun. These, then, upon return to the environment of origin, could have exerted a synchronizing effect upon those more labile functions whose phase had shifted, and, if sufficiently dominant, such an effect could have accelerated the back shift to the extent demonstrated.

V. Summary and Conclusions.

At periodic intervals throughout the biological day, biomedical assessments were made for a week prior to jet flight to Manila, for 8 days of layover at Manila, and for a week following return to the environment of origin. From the obtained data, the following conclusions were derived:

(1) Rapid translocation through the 10 time zones effected a primary shift of phase of the circadian periodicity manifested by the physiological functions assessed. For rectal temperature and heart rate, the time required for completion of phase shift was approximately 4 days, and for palmar evaporative water loss, approximately 8 days.

(2) Return back to the environment of origin also effected a shift of phase that required no more than 1 day for completion.

(3) Behavioral integrity was degraded during the primary period of transition and, to a lesser extent, during the period of transition occasioned by return to the environment of origin.

(4) Duration of behavioral impairment was much shorter than the lag time of physiological phase shifts.

REFERENCES

1. ADAMS, T., FUNKHOUSER, G. E., and KENDALL, W. W.: Measurements of Evaporative Water Loss by a Thermal Conductivity Cell. *J. Appl. Physiol.*, 18: 1291–1293, 1963.
2. ADAMS, T., FUNKHOUSER, G. E., and KENDALL, W. W.: A Method for the Measurement of Physiological Evaporative Water Loss. CARI Report No. 63–25, Federal Aviation Agency, 1963.
3. ASCHOFF, J., and WEVER, R.: Spontanperiodik des Menschen bei Ausschluss aller Zeitgeber. *Naturwissenschaften*, 49: 337–342, 1962.
4. BROZEK, J., SIMONSON, E., and KEYS, A.: Changes in Performance and in Ocular Functions Resulting from Strenuous Visual Inspection. *Amer. J. Psychol.*, 63: 51–66, 1950.
5. BUGARD, P., and HENRY, M.: Quelques Aspects de In Fatigue dans Aviation de Transport. *La Presse Medicale*, 69: 1903–1906, 1961.
6. BUNNING, E.: The Physiological Clock. Academic Press, Inc., New York, 1964.
7. BURTON, A. C.: The Clinical Importance of the Physiology of Temperature Regulation. *Canad. Med. Assoc. Journal*, 75: 715–720, 1956.
8. FLINK, E. B., and DOE, R. P.: Effect of Sudden Time Displacement by Air Travel on Synchronization of Adrenal Function. *Proc. Soc. Exptl. Biol.* (New York), 100: 498–501, 1959.
9. GERRITZEN, F.: The Diurnal Rhythm in Water, Chloride, Sodium, and Potassium Excretion During a Rapid Displacement from East to West and Vice Versa. *J. Aerospace Med.*, 33: 697–701, 1962.
10. HAUTY, G. T.: Relationships Between Operator Proficiency and Effected Changes in Biological Circadian Periodicity. *J. Aerospace Med.*, 34: 100–105, 1963.
11. HAUTY, G. T., and ADAMS, T.: Phase Shifting of the Human Circadian System. In Circadian Clocks, J. ASCHOFF, ed. North-Holland Publishing Co., Amsterdam, 1965.
12. KLEITMAN, N.: Sleep and Wakefulness. Univ. of Chicago Press, Chicago & London, 1963.
13. LEWIS, P. R., and LOBBAN, M. C.: Dissociation of Diurnal Rhythms in Human Subjects Living on Abnormal Time Routines. *J. Exptl. Phys.*, 42: 371–386, 1957.
14. MEAD, J., and BOMMARITO, C. L.: The Reliability of Rectal Temperature as an Index of Internal Body Temperature. *J. Appl. Physiol.*, 2: 97, 1949.
15. PEARSON, R. G., and BYARS, G. E.: The Development and Validation of a Checklist for Measuring Subjective Fatigue. USAF Report No. 56–115, School of Aviation Medicine, 1956.
16. SASAKI, T.: Effect of Rapid Transposition Around the Earth on Diurnal Variation in Body Temperature. *Proc. Soc. Exptl. Biol. Med.*, 115: 1129–1131, 1964.

66–4345