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

II. West-East Flight

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Released by

P. V. SIEGEL, M.D.
FEDERAL AIR SURGEON

December 1965

FEDERAL AVIATION AGENCY

Office of Aviation Medicine

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I. Introduction.

As reported,[4] biomedical assessments were made on human subjects throughout a week prior to jet flight to Manila, during 8 days of layover in Manila, and for a week following return to Oklahoma City. It was found that the lag time of the circadian phase shift manifested by rectal temperature and heart rate was approximately 4 days and, by palmar evaporative water loss, approximately 8 days. In contrast, shift in phase effected by return to Oklahoma City required only 1 day. 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, but duration of behavioral impairment was much shorter than the lag time of physiological phase shifts.

Data to be reported here were obtained from a subsequent jet flight to Rome, Italy, designed to reveal differential effects of East-West and West-East time displacement.

II. Method.

A. *Flight.* Time of departure (Oklahoma City) was 1400 hours (CST), total time in transit 15-½ hours, arrival time (Rome) was 1230 hours local time, and time displacement was 7 hours.

B. *Schedule of Assessment.* As in previous testing,[4] periodic biomedical assessments were made on alternate days during the week immediately prior to flight, during a 12-day period in Rome, and during the week following return to Oklahoma City. Throughout each test day, assessments were repeated at 0700, 1100, 1500, 1900, and 2300 hours (local time). During each of these five periods of assessment, several different psychological functions were sequentially assessed by standardized procedures. Simultaneously, measurements were also made of physiological functions. The time required for such a period was approximately 25 minutes.

C. *Assessments.* The following assessments were made.

1. *Rectal Temperature.* Internal body temperature was measured by a portable, indicating bridge circuit, calibrated to a thermistor rectal probe that 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 1-hour 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,[2] 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 period, indicating both steady-state "basal" levels during rest and increased evaporative rates during assessment. These data were examined to provide: (1) measurements of "basal" evaporative water loss; (2) increases in instantaneous rates related to matched assessments; and (3) the total amount of water evaporated during the entire assessment period and its individual subcomponents.

3. *Heart Rate and Respiratory Rate.* A lightweight, plastic and elastic chest strap was improvised to house three silver electrodes for heart-rate measurement 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. *Blood Pressure.* Blood pressure was measured periodically throughout each assessment period by standard auscultatory techniques, using an inflatable arm cuff and indicating sphygmomanometer; both systolic and diatolic pressures were recorded.

5. *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.

6. *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.

7. *Critical Flicker-Fusion.* Three ascending and three alternating descending thresholds were determined by an International Applied Science Laboratory apparatus (FP104 frequency and program module and OFC–3 optical unit). 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.

8. *Numerical Ability.* This was measured by a 90-item, 3-minute test requiring the addition of one- and two-digit numbers in sets of three (RPM Number Facility—NF—Alternate Forms—1959 edition published by the Hogg Foundation, University of Texas). The score represents a relatively factor-pure measure in speed and accuracy of simple addition.

9. *Subjective Fatigue.* The level of subjective fatigue was measured by means of checklists, developed by the scale-discrimination method, which were shown to reflect significantly the effects of perceptual-motor work and pharmacological treatment.[5]

D. *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 postreturn 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.* Data obtained during preflight (Oklahoma City) and postflight (Rome) days of assessment are given in Figure 1. For each function, plotted values are the means of the four subjects for each hour for rectal temperature, for each assessment period for palmar evaporative water loss, blood pressure, heart rate, and respiratory rate, and for each day of assessment for the psychological functions. Preflight values represent the pooled means of the four subjects for the last 2 days of preflight assessment 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. During the first day in Rome (Day +1), essentially the same form of curve is seen, suggesting that a complete shift in phase was achieved. It should be remembered, however, that time of arrival in Rome was 1230 hours (Rome time), and so it is most probable that the phase of the period was still set to Oklahoma City time. On Day +2, the predicted phase lag is demonstrated. A precise determination of the number of days required for the completion of the shift of phase to the local time of Rome cannot be made owing to the variability of the subsequent rectal-temperature curves, which, for Day +3, is most marked. It does appear though that shift of phase was not completed prior to Day +6.

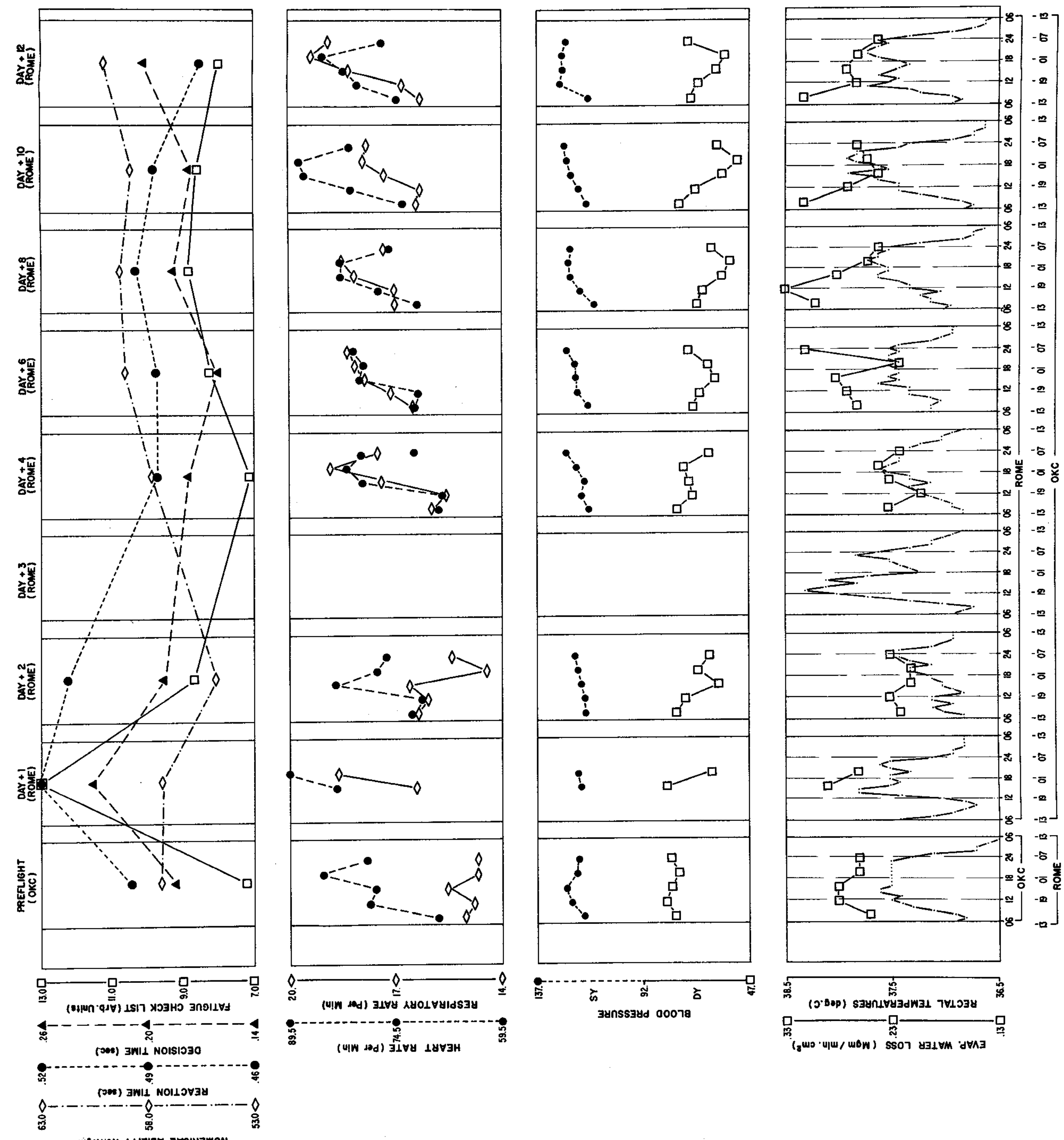

FIGURE 1. Mean plottings of data obtained in Oklahoma City (preflight) and in Rome (layover).

2. *Palmar Evaporative Water Loss.* Plotted with the rectal-temperature curves in Figure 1 are mean values for resting palmar evaporative water loss. 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 in that no consistent form of periodicity is manifested by palmar evaporative water loss during any of the days in Rome.

Since assessments were made only during the 1500- and 1900-hour periods on Day +1 for the East-West flight, a similar schedule was required for the flight being reported.

3. *Blood Pressure.* During preflight, systolic pressures evidence a circadian periodicity referenced to local time, whereas diastolic pressures do not. Yet, beginning with Day +6, periodicity is consistently demonstrated by the diastolic-pressure curves. In contrast, the subsequent curves of systolic pressure do not show clearly a return to the periodicity noted during preflight.

4. *Heart Rate.* Circadian periodicity is also revealed by the preflight values plotted for heart rate, and its phase also is seen to be closely associated with that of internal temperature. Its time lag, however, may be somewhat longer since a complete shift of phase does not appear to occur until Day +8.

5. *Respiratory Rate.* In contrast to heart rate, respiratory rate does not demonstrate a well-defined or consistent periodicity except for the last 3 days in Rome.

6. *Numerical Ability.* Despite a considerable amount of practice given prior to the preflight period of assessment, the effect of practice is clearly eivdent up to the last day in Rome (Day +12). Against this trend of gradual improvement, it is difficult to detect deficit except for Day +2, which does show clearly a decrement.

7. *Reaction Time.* 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 preflight values for comparison, reaction time is seen to increase substantially (i.e., become slower) during Day +1 and also Day +2. On Day +3, reaction time decreases (improves in speed) to slightly below preflight levels. Analyses of the variance attributable to replicated days of assessment reveal that the increment of reaction time on Day +1 and Day +2 is not statistically significant.

8. *Decision Time.* The values plotted for decision time in Figure 1 represent the daily mean speed of decision as defined. As for reaction time, decision time increases (becomes slower) on Day +1, returns toward the preflight level on Day +2, and, except for Day +12, remains about this level for the remaining days of assessment in Rome. In using the above-mentioned model for analysis of variance, the increase in decision time noted for Day +1 was not statistically significant.

9. *Subjective Fatigue.* The index of subjective fatigue was scaled from "extremely fatigued" to "extremely alert"; the higher the daily mean values plotted in Figure 1, the more fatigued the subjects felt themselves to be. The level of fatigue reported by the subjects is seen to be high on Day +1, lower on Day +2, and, on Day +4, equal to the level reported during preflight. This demonstrated increment in fatigue was found to be highly significant ($P=0.001$).

10. *East-West and West-East Comparison.* In Figure 2 are plotted hourly rectal-temperature recordings obtained from two subjects (CC and TB) who participated in both flights (Manila and Rome). Missing data for TB are attributable to the interference of the technical duties that this particular subject had to perform. Inspection of TB's rectal-temperature curve for the first and seconds days in Rome reveals the opposable lags demonstrated by Figure 1. Completion of the phase shift is shown on Day +6. In Manila, the curves of this subject are characterized by the expected lag to the left on Days +1 and +2. Completion of the phase shift, however, is difficult to determine because of the marked increase in amplitude seen to occur in Day +6. Nevertheless, the probable time for the phase shift is not appreciably different from that of the flight to Rome. Essentially the same form of curves was obtained from subject CC; shift of phase appears to have been completed on Day +6 in Rome and, perhaps, on Day +4 in Manila.

B. *Back Shift.* Time of departure for the return flight to Oklahoma City was 1300 hours (Rome time), total time in transit was 18-½ hours, and arrival time was 0030 hours (CST). The first day of postflight assessment followed the day of arrival in Oklahoma. This difference must be taken into account when comparing the primary and back shifts.

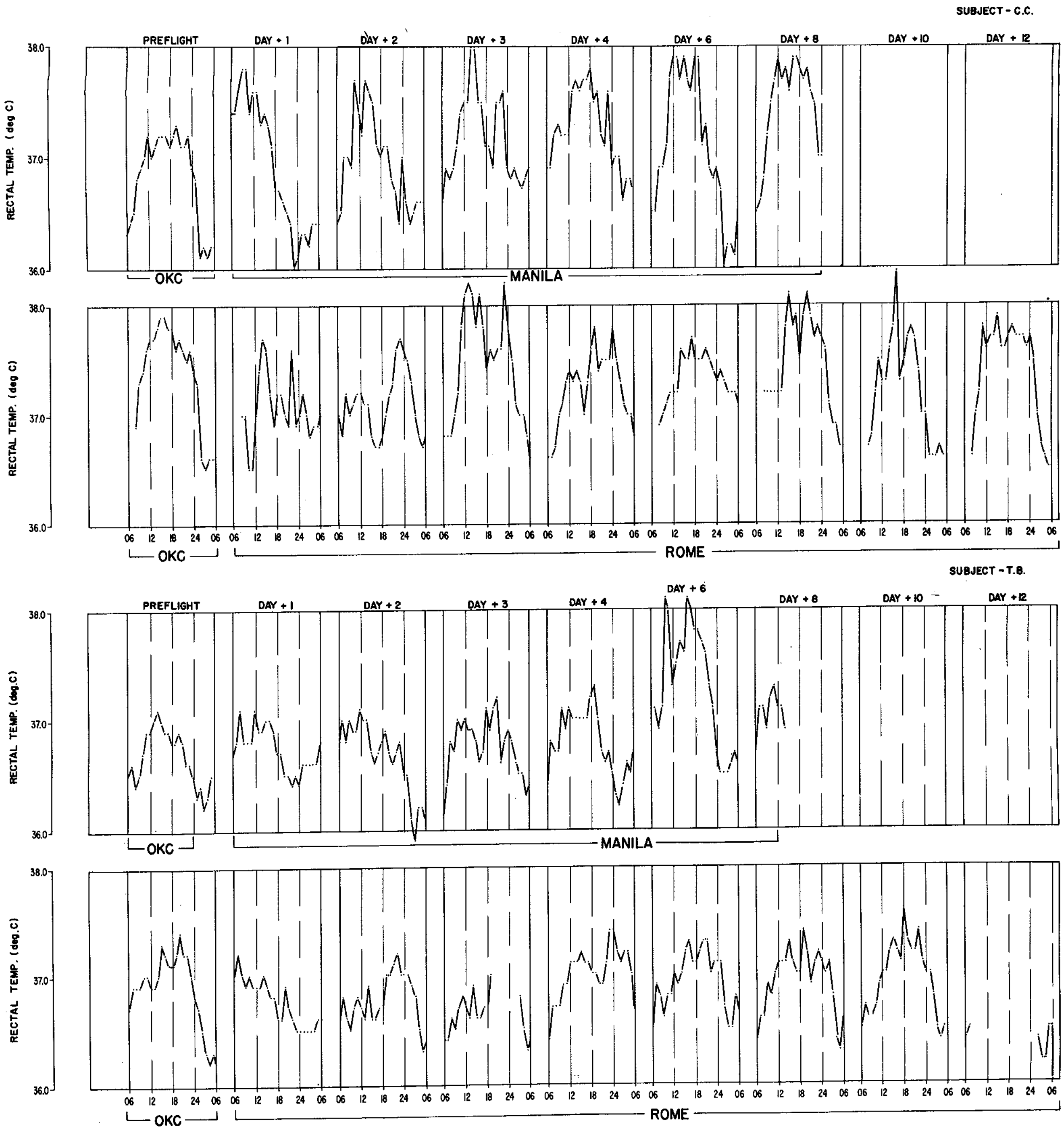

FIGURE 2. Rectal-temperature recordings obtained in Oklahoma City and overseas from two subjects who participated in the East-West and West-East flights.

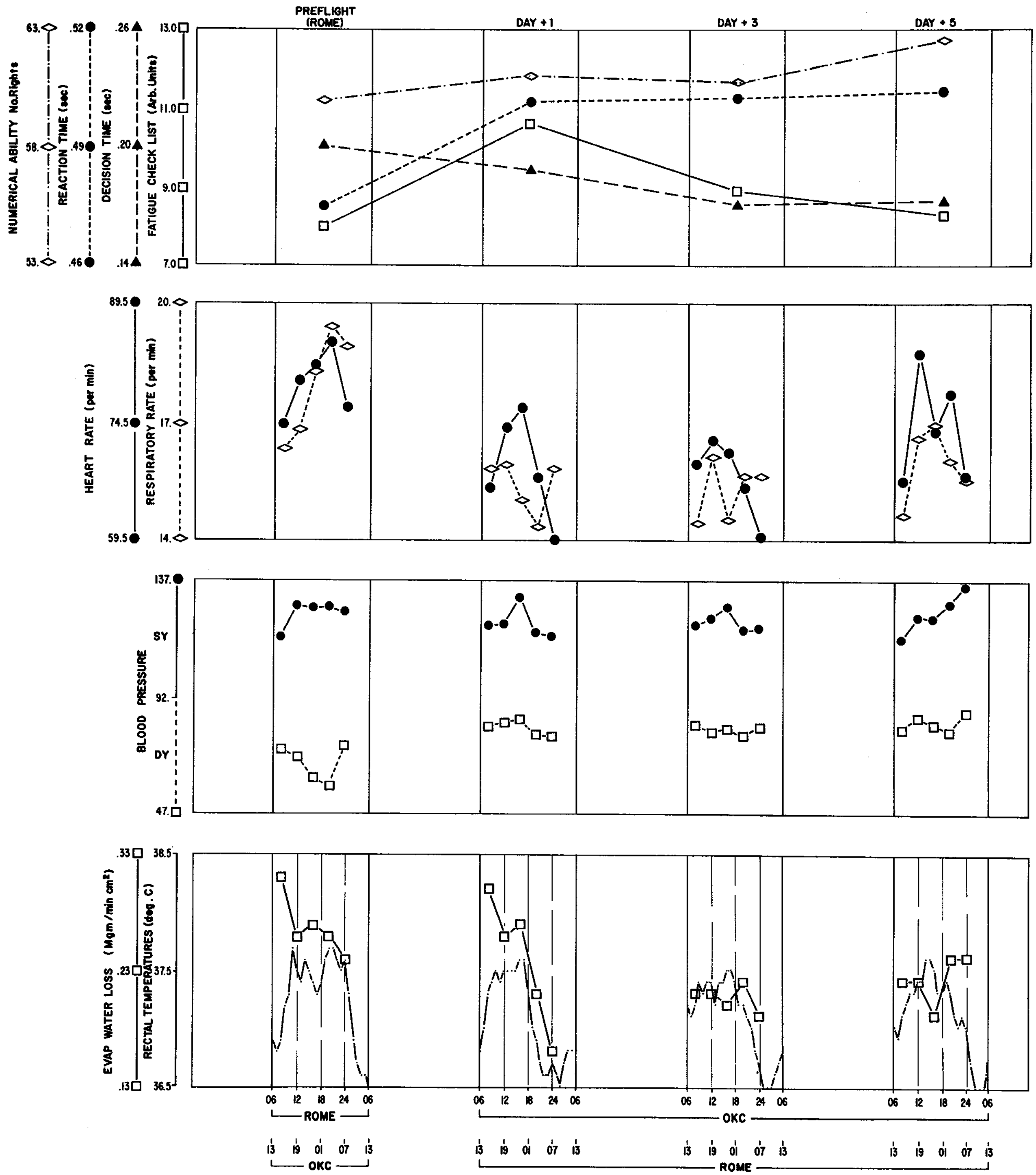

Figure 3. Mean plottings of data obtained in Rome (preflight) and in Oklahoma City (return flight).

Figure 3 presents data for determining the effects of time displacement occasioned by the flight back to Oklahoma City.

1. *Physiological Functions.* Circadian periodicity appears to be sustained for only two of the functions assessed, rectal temperature and heart rate. For both, a complete phase shift back to the local time of Oklahoma is not shown by any of the postflight days of assessment.

2. *Psychological Functions.* A pronounced increase in reaction time is shown by Day +1, and this increment persists during the remaining days of assessment; however, this increment is not statistically significant. Increase in fatigue is reported on Day +1 ($P=0.001$) but on Day +5, fatigue has returned to the level reported during preflight. In contrast, decision time decreases slightly but not statistically significantly during Days +1 and +2.

3. *Comparison of East-West and West-East Back Shifts.* Rectal temperatures obtained from subjects CC and TB following return to Oklahoma City are presented by Figure 4. For TB, the phase lag is seen to persist through Day +5 following return from Rome; following return from Manila, the phase lag is equally persistent. Interpretation is difficult owing to the substantial difference in the time of day that temperature peaks during the two preflight assessments (Rome and Manila). Phase lag is also revealed by the curve of CC following his return from Rome, and this persists through Day +5. In contrast, a complete shift of phase would appear to have occurred following his return from Manila.

IV. Discussion.

Interpretation of the bidirectional effects of time displacement reported here and earlier [4] must take into consideration the influence of individual differences and of voluntary activity associated with the attempt to retain normal living habits throughout the course of biomedical assessment. As has been revealed, mean values of rectal temperature obtained in Rome indicate that phase shift did not appear complete until Day +6. In comparison, it was found that the shift of phase was completed on Day +4 in Manila.[4] Within the limits of the two factors mentioned above, phase shifts for East-West and West-East displacements may be the same.

The differential time lag of the primary phase shifts manifested by the periodicity of heart rate during the two flights may also be attributable to the same factors; however, the lag difference is more extreme. In Rome, phase shift was not complete until Day +8, whereas, in Manila, shift of phase was completed on Day +4. In Rome, heart rate and rectal temperature were dissociated with respect to phase, whereas, in Manila, the phases of heart rate and rectal temperature were not dissociated during the period of transition. If this is a real bidirectional difference, an explanation is not available.

A more notable difference between the East-West and West-East flights is that revealed by psychological deficit and its duration. The curves of reaction time, decision time, and subjective fatigue obtained in Rome show a high degree of agreement with those of the Manila flight; that is, increase in each of these three functions occurs on Day +1, but this increase or deficit is of very short duration in comparison with the time lags seen for the physiological functions. For the Rome flight, however, tests of statistical significance indicate that only the increment in fatigue can be accepted as a real or experimentally induced difference, suggesting that, despite increased subjective fatigue, psychological performance was unaffected by the joint effects of time displacement and prolonged flight. Why psychological deficit occurred in Manila but not in Rome may be answered by the flight yet to be reported, which was designed to appraise the effects of prolonged flight alone.

The most apparent notable difference, perhaps, is revealed by the back shift. Here, following return from Rome, a complete shift of phase was not revealed by any of the physiological functions during any of the days of postflight assessment. Following return from Manila, a complete shift of the phase of rectal temperature was seen on Day +1. Since such a bidirectional difference is difficult to reconcile with the probability that little or no bidirectional difference may exist between the primary phase shifts of rectal temperature, the temperature recordings of each subject were individually inspected. It was found that a complete back shift of phase did occur in the case of two subjects but not for the other two. This does not resolve the question of bidirectional difference. It does indicate, however, that even for those functions manifesting periodicity of assumed stability, larger samples of subjects are required.

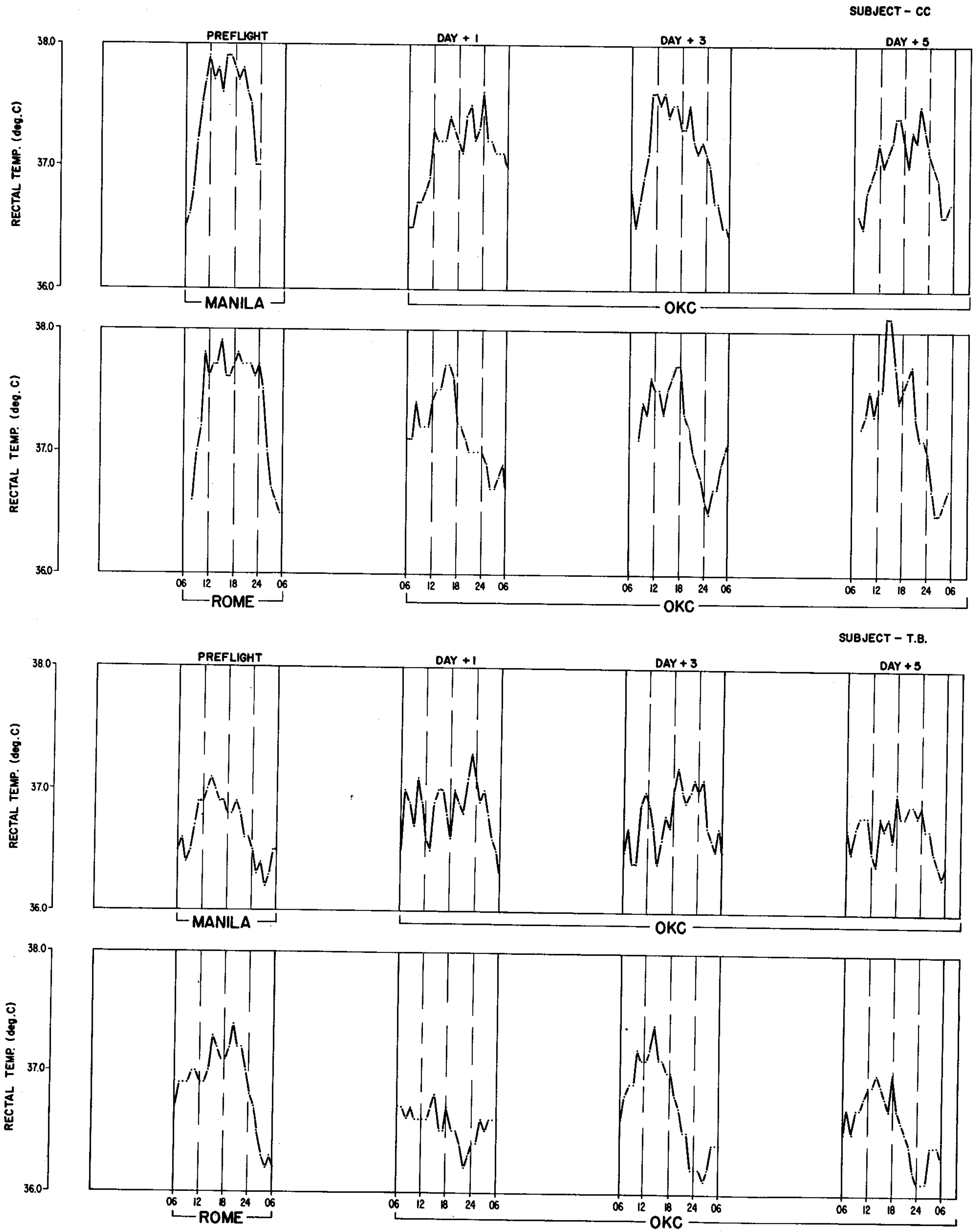

FIGURE 4. Rectal-temperature recordings obtained on last day overseas (preflight) and following return to Oklahoma City.

V. Summary and Conclusions.

At periodic intervals throughout the biological day, biomedical assessments were made for a week prior to jet flight to Rome, for 12 days at Rome, and for a week following return to Oklahoma City. The following conclusions were derived:

(1) Rapid translocation through the seven time zones effected a primary shift of phase of the circadian periodicity manifested by physiological functions. For rectal temperature and heart rate, the time required for completion of phase shift was from 4 to 6 days and 6 to 8 days, respectively.

(2) Return back to the environment of origin also effected a shift of phase manifested by internal temperature that, for two subjects, was completed in less than 5 days and, for the two remaining subjects, was not completed in 5 days.

(3) Increase in fatgue occurred during the primary period of transition and following return to the environment of origin, but psychological performance was not impaired during either period.

(4) Duration of the fatigue was shorter than the time lag of the physiological phase shifts.

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U.S. GOVERNMENT PRINTING OFFICE: 1966 O—211-396