REPORT DOCUMENTATION PAGE	1. REPORT NO.	2.	PB89-227870
4. Title and Subtitle Physiological Adaptation of Shift Workers			5. Report Date 77/00/00
			6.
7. Author(s) Weitzman, E. D.			8. Performing Organization Rept. No.
9. Performing Organization Name and Address Department of Neurology, Montefiore Hospital and Medical Center, Bronx, New York			10. Project/Task/Work Unit No.
			11. Contract (C) or Grant(G) No. (C) (G) R01-OH-00331
12. Sponsoring Organization Name and Address			13. Type of Report & Period Covered
			14.

15. Supplementary Notes

16. Abstract (Limit: 200 words) Health workers in a large municipal hospital participated in this study to define the mode of adaptation of several important physiological measures to acute and chronic sleep/wake cycle shifts in shift workers. The study was divided into two parts: an acute shift work reversal protocol and a more chronic reversal group. A total of nine subjects (eight nurses and one intern) participated. Polygraphic sleep stage patterns, plasma cortisol, body temperature curves, and growth hormones were sampled over several selected 24 hour periods. The findings suggest that a significant and persistent decrement of sleep amount, organization and stability occur when hospital workers assume a night shift schedule. The major effect was a decrease in total sleep time, an increase in sleep stage shifts, and decreases in the minutes spent in both rapid eye movement (REM) and Stages 3 and 4 of sleep. However, the percentage of the sleep occupied by REM, Stage 2 and Stage 3 remained rather constant. Changes in cortisol indicated that the circadian rhythm of secretion was clearly changed during the night work schedule although no mean concentration differences were noted. Following sleep onset there was a consistent decrease in the cortisol concentration, independent of the time of day. In general, the change to an acute shift work schedule produced major changes in sleep patterns and cortisol and growth hormone secretions. These changes did not adapt, but appeared to become more abnormal after 2 weeks.

17. Document Analysis a. Descriptors

b. Identifiers/Open-Ended Terms NIOSH-Publication, NIOSH-Grant, Grant-Number-R01-OH-00331, End-Date-05-31-1976, Grants-other, Shift-work, Health-care-personnel, Nursing, Physicians, Hormone-activity

c. COSATI Field/Group

18. Availability Statement	19. Security Class (This Report)	21. No. of Pages 50
	22. Security Class (This Page)	22. Price

Grant # RØ1-OH-ØØ331

Summary Progress Report (OHS 00331) 7/1/74 - 12/31/76

"Physiological Adaptation of Shift Workers"

Elliot D. Weitzman, M.D., Principal Investigator
Montefiore Hospital & Medical Center

INTRODUCTION:

The primary objective of the research is to define the mode of adaptation of several important physiological measures to acute and chronic timed sleep-wake cycle shifts in "working" shift-work subjects. We particularly chose health workers in a large municipal hospital. The study was divided into two parts. An acute shift-work reversal protocol and a more chronic-reversal group. In our original proposal we had hoped to study a total of 15 medical interns and 15 nurses during a period of 3 years. However, it was recommended by NIOHS staff, that medical interns not be studied since they might not be considered typical of a "shift-work" group. We therefore restricted our study to nurses (although we did study one medical intern). In addition, the length of the research grant was reduced to 2 years. (We obtained administrative approval to extend the study for an additional 6 months, but with no additional funds). Finally, the budget support for each of the two years was reduced to approximately 50% of our original request. In spite of these serious constraints on our research proposal, we nevertheless were able to successfully study a total of 9 subjects (8 nurses, 1 intern). Seven were evaluated in the "Acute Reversal Protocol (Part I), Table 1 and two in the "Chronic Reversal Protocol" (Part II). The major emphasis of this study was to determine the effect of a work related phase-shift in a series of individuals with detailed longitudinal physiological measurements. We therefore studied the following variable, polygraphic sleep stage patterns, frequently sampled plasma cortisol and growth hormones over several selected 24 hour periods and 24 hour body temperature curves.

addition on the day of blood sampling, although a technician was with the subject to draw the samples every 20 minutes, minimal interference occurred in regard to their work duties. Thus we obtained a total of approximately twelve sleep records (total of approximately 84 sleep hours) and approximately 225 plasma samples per subject. The polygraphic sleep records are "hand" scored minute by minute using the standard "Rechtschaffen and Kales" sleep scoring Manual ( ). The hormones (cortisol and growth hormone) were analyzed, each in duplicate using standard micro-competitive protein binding and radioimmunoassay techniques (a total of approximately 1000 assays were therefore measured on each subject).

All the sleep scored data and plasma hormonal assays have now been completed and transferred to the data base of our computer system (HP 2100).

The following data analysis has been carried out for each of the subjects in the Part I protocol.

1) Minute by minute analysis of sleep stage patterns including total minutes and percent of stage sleep and total time for each sleep recording.

2) Means and S.D. of minutes of each stage for each consecutive hour for each sleep recording.

3) Frequencies of sleep stage sequences for each sleep recording expressed as minutes and percent

4) A chronograph plot (cal-comp, HP 2100) of each 24 hour day depicting the graphic display of the sequence of sleep stages, and waking as a function of clock time.

Part II Chronic Shift Protocol

We have studied only 2 subjects in this portion of the study because of limitations of time and funding. However, data analysis has been complete for all sleep patterns and hormonal assays for these two subjects. The protocol completed for subjects B.B. and J.M. was to obtain all sleep patterns on four sequential 24 hour periods and to obtain 20 minute plasma samples on the 4th 24hour period. Both of these subjects were chronic night shift workers, (B.B. for 10 years and J.M. for 1½ years).

percent of total sleep time (18%, 17% and 17% for the 3 sequential recorded sections) (Table 5). This preservation of the REM percent was, of course, accompanied by a decrease of REM time in minutes of 64, 47 and 41 minutes respectively for each section of the study (Table 6). There was a tendency to maintain total Stage 3 and 4 (Tables 7 and 8). Thus the baseline mean value of 81 minutes of Stages 3 and 4 was succeeded by 68 and 58 minutes during the sleep periods on the night shift, with 23% of total sleep spent in Stage 3 and 4 in baseline, and 23 and 25% respectively for the beginning and end of the acute shift work schedule. Stage 2 percent of total sleep was essentially unchanged throughout the study with values of 54, 55 and 53% (Table 9). An interesting statistic is the increase in number of sleep stage changes during the night shift work period (Table 10). This indicates that sleep was less stable and that more frequent state changes occurred when on the night shift, as compared to day shift.

A graphic display of the cumulative pattern of sleep stages REM and Stages 3 and 4 as a function of elapsed sleep time is summarized in Graphs 1 and 2 for baseline and the phase shift periods. These graphs demonstrate that the rate of accumulation of Stages 3 and 4 is remarkably the same until approximately 2 hours of sleep and then diverge primarily as a function of total sleep time, the least cumulative amount occurred during the second week after the acute shift to the night work schedule and the greatest amount was present in the baseline pre-shift nocturnal sleep period (Graph 1). However, a clearly different cumulative rate was present for REM sleep (Graph 2). The slope of the cumulative REM sleep curve was greater in the first 3 hours after sleep onset during the second week of night work, but then rapidly deaccelerated and reached a plateau, reaching only about 50% of total REM time as compared with the baseline values.

subjects studied who were on "long term" night work schedules. In this very demanding protocol, we only missed one 24 hour blood sampling of one subject (L.O.) on the third 24 hour period. On one subject (P.F.) we also obtained a fourth 24 hour sampling one week after he had returned to a day work-night sleep schedule. We therefore completed a total of 23 - twenty-four hour blood sampling protocols, (total of approximately 1,680 plasma samples). All of the plasma cortisol assays were done in duplicate in our laboratory using a micro-competitive protein binding assay. The Growth Hormone was assayed with a radio-immunoassay.

I include the computer plotted graphs of all the 24 hour cortisol, Growth Hormone and the concomitant sleep stage patterns (Graphs 3-26). In addition, we obtained graphs of the mean percent deviation of the cortisol data in the three conditions, baseline, early night-work shift and later night-work shift as a function of clock time (Graphs 27-29). We have also obtained a similar percent deviation 24 hour plot of the pattern in relation to sleep onset rather than clock time for the early and later shift 24 hour patterns (Graphs 30,31).

Preliminary analysis of these results leads to the following tentative interpretations:

1) Baseline (pre-shift) 24 hour cortisol patterns are essentially the same in hospital workers as the general population we have studied and therefore serves as an appropriate control for the effects of acute and chronic shift on night-work schedules.

2) Several days after shift to a night-work schedule, a clear change in the 24 hour circadian episodic pattern of cortisol takes place, such that the nocturnal fall is less prominent, the uni-modal rhythmic 24 hour

acute shift study only 2 subjects had a prominent sleep related release on both 24 hour samplings. Estimates of the mean HGH concentration over 24 hours for the group as a whole showed that although there was no change between baseline and the "begin" shift measurement (0.40 and 0.45 ng/ml repectively) there was a large decrease in the "end" shift value 0.16 ng/ml (Table 12). This was also the case for the estimate of the <u>peak</u> HGH value obtained during the first 4 hours after sleep onset (Table 13). The mean value fell from 6.31 in baseline to 2.74 and 1.02 ng/ml in the "begin" and "end" shift 24 hour measurements.

In general, the assumption of an acute shift-work schedule by hospital workers produced major changes in sleep patterns and cortisol and Growth Hormone 24 hour secretions. These alterations did not adapt but in fact appeared to become more abnormal after 2 weeks, when compared with the baseline values.

Further data analysis, especially for the body temperature measurements and subjective daily questionnaire responses will be analyzed and, when obtained, the results will be sent to NIOSH as an addendum.

TABLE 4

Mean % REM in first 3 Hours of Total REM for entire sleep period

Baseline	26%
Begin	49%
End	65%

TABLE 5

REM % Mean all subjects		Subjects 1	2	3	4	5	6	7
Baseline	18	21	13	23	17	20	19	7
Begin	17	24	11	22	20	14	17	7
End	17	27	17	17	15	20	18	7

TABLE 6

Total REM Time (Mins) Mean all subjects		Subjects 1	2	3	4	5	6	7
Baseline	64	62	43	85	61	81	73	29
Begin	47	63	26	61	77	37	41	29
End	41	78	24	40	44	42	36	23

TABLE 10

	Total # of Stage Changes	Total # Mins.	Stage Change/Min	Per Hr.
Baseline	933	2497	.37	22.2
Begin	893	1989	.45	27.0
End	830	1702	.49	29.4

TABLE 11

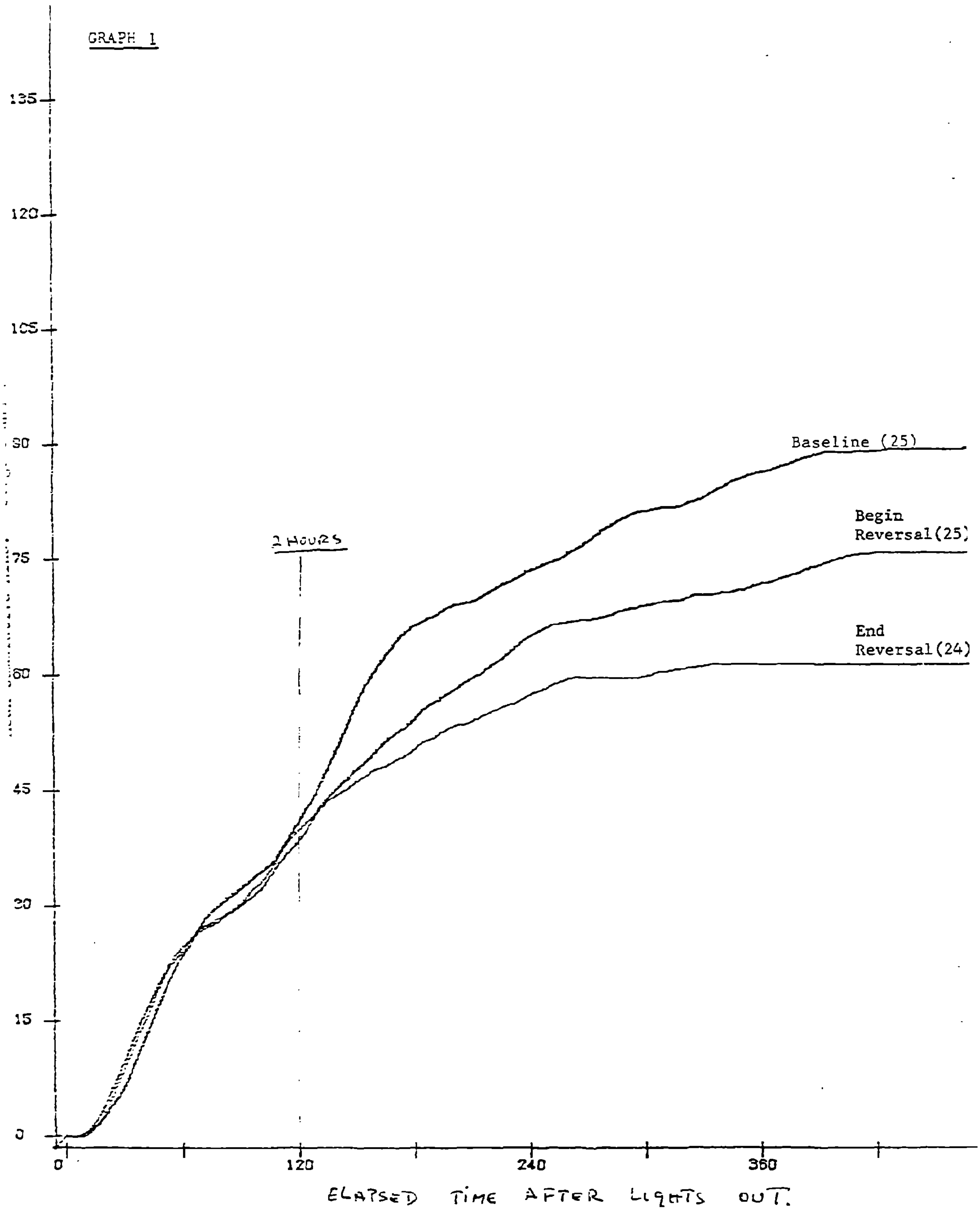
Cortisol Mean Concentration/24 hours (ug/100ml)

		Subjects						
	overall $\bar{x}$	1	2	3	4	5	6	7
Baseline	7.1	5.3	7.1	9.1	6.0	7.6	6.3	8.5
Begin	7.6	6.6	7.6	7.7	4.5	-	7.8	11.3
End	7.9	5.7	6.5	8.3	8.2	-	8.6	10.1

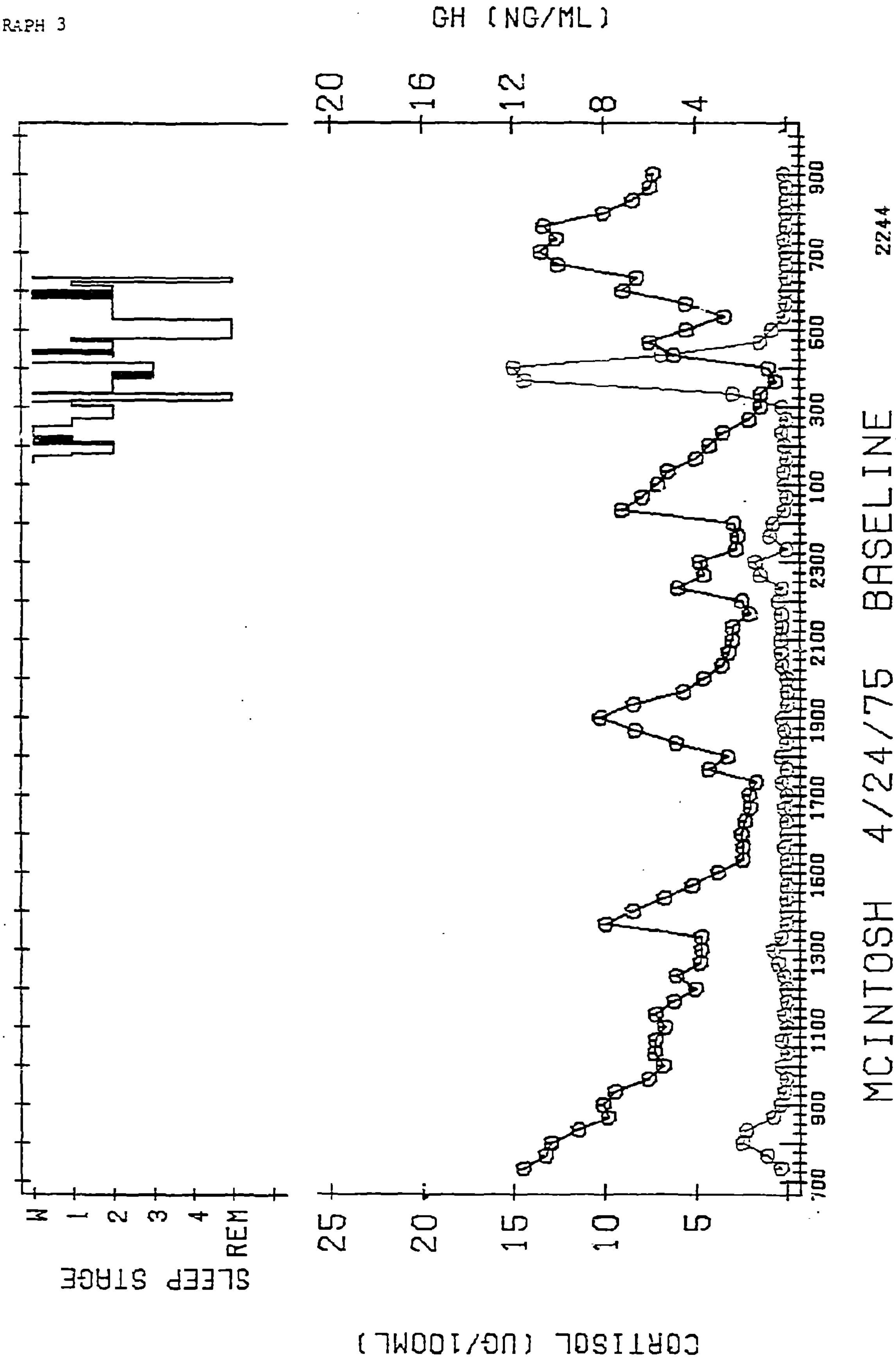
TABLE 12

Growth Hormone Mean Concentration/24 hrs. (ng/ml)

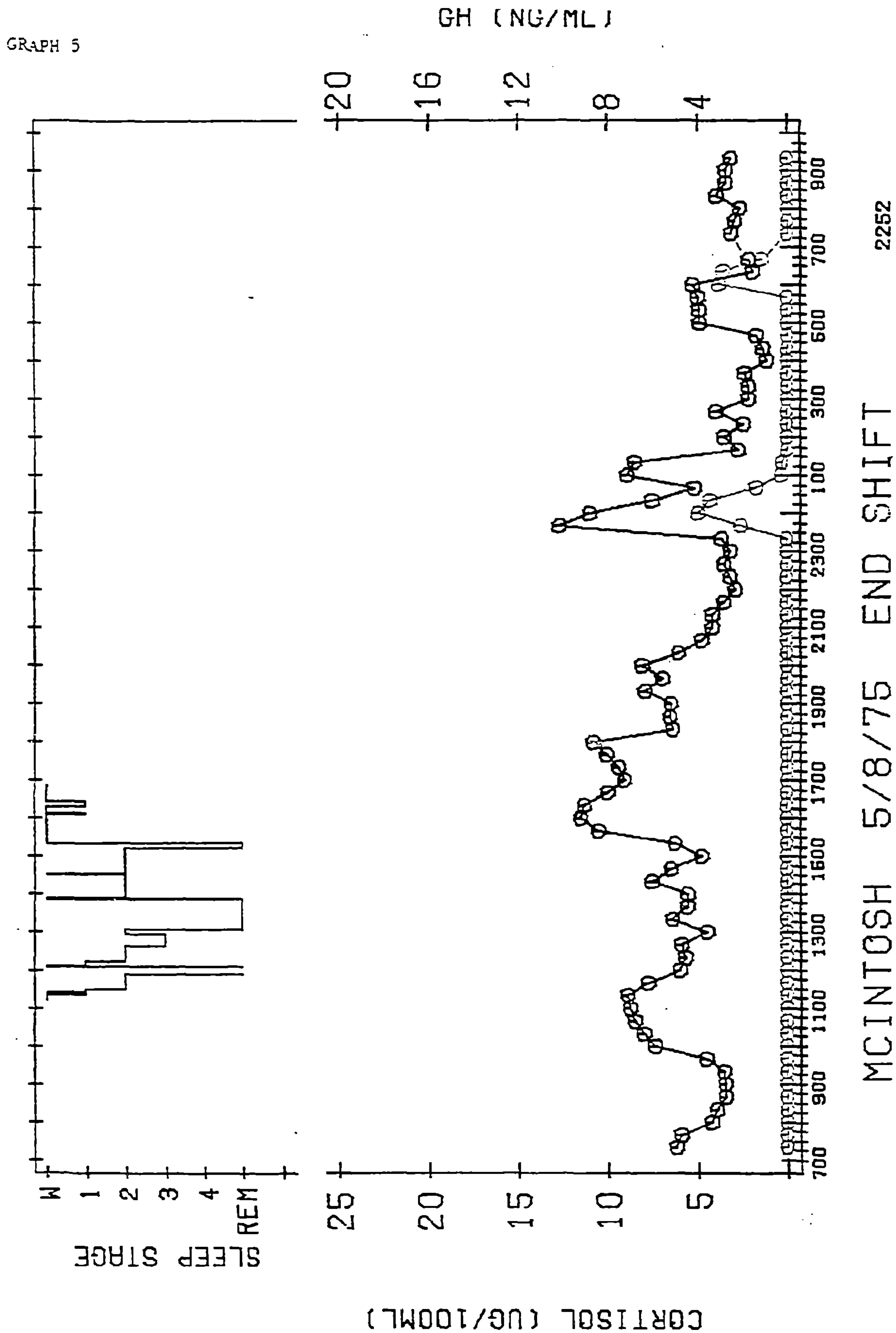
		Subjects						
	overall $\bar{x}$	1	2	3	4	5	6	7
Baseline	.40	.60	.01	.51	.12	.12	1.31	.10
Begin	.45	.74	.10	.88	.48	-	.41	.09
End	.16	.26	.04	.19	.05	-	.47	.00


GRAPH 1
135
120
105
90
75
60
45
30
15
0
2 HOURS
Baseline (25)
Begin Reversal(25)
End Reversal(24)
0
120
240
360
ELAPSED TIME AFTER LIGHTS OUT.

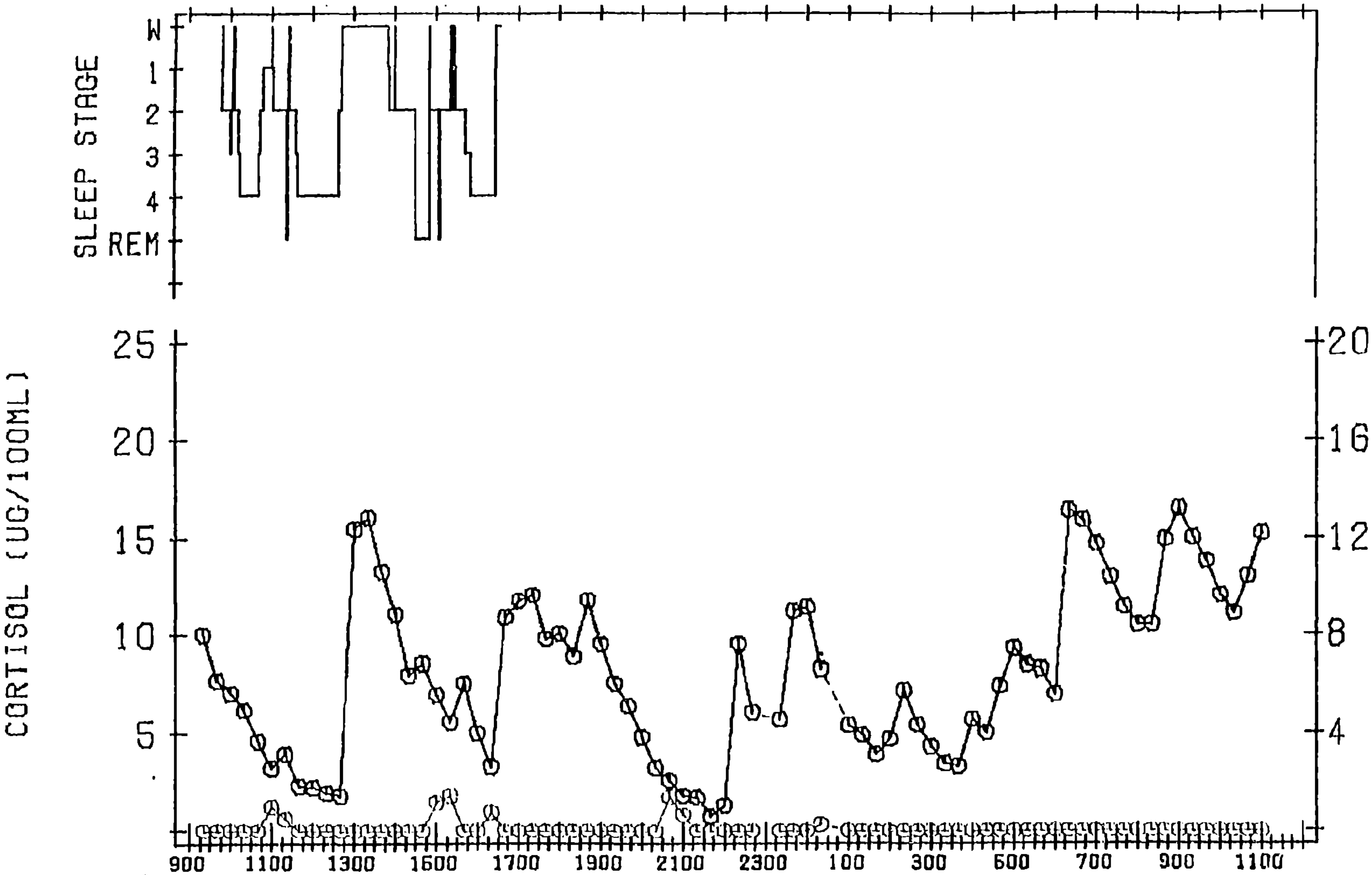
GRAPH 3



MCINTOSH 4/24/75 BASELINE
GH (NG/ML)
CORTISOL (UG/100ML)
SLEEP STAGE
W
1
2
3
4
REM
25
20
15
10
5
20
16
12
8
4
700
900
1100
1300
1500
1700
1900
2100
2300
100
300
500
700
900
2244

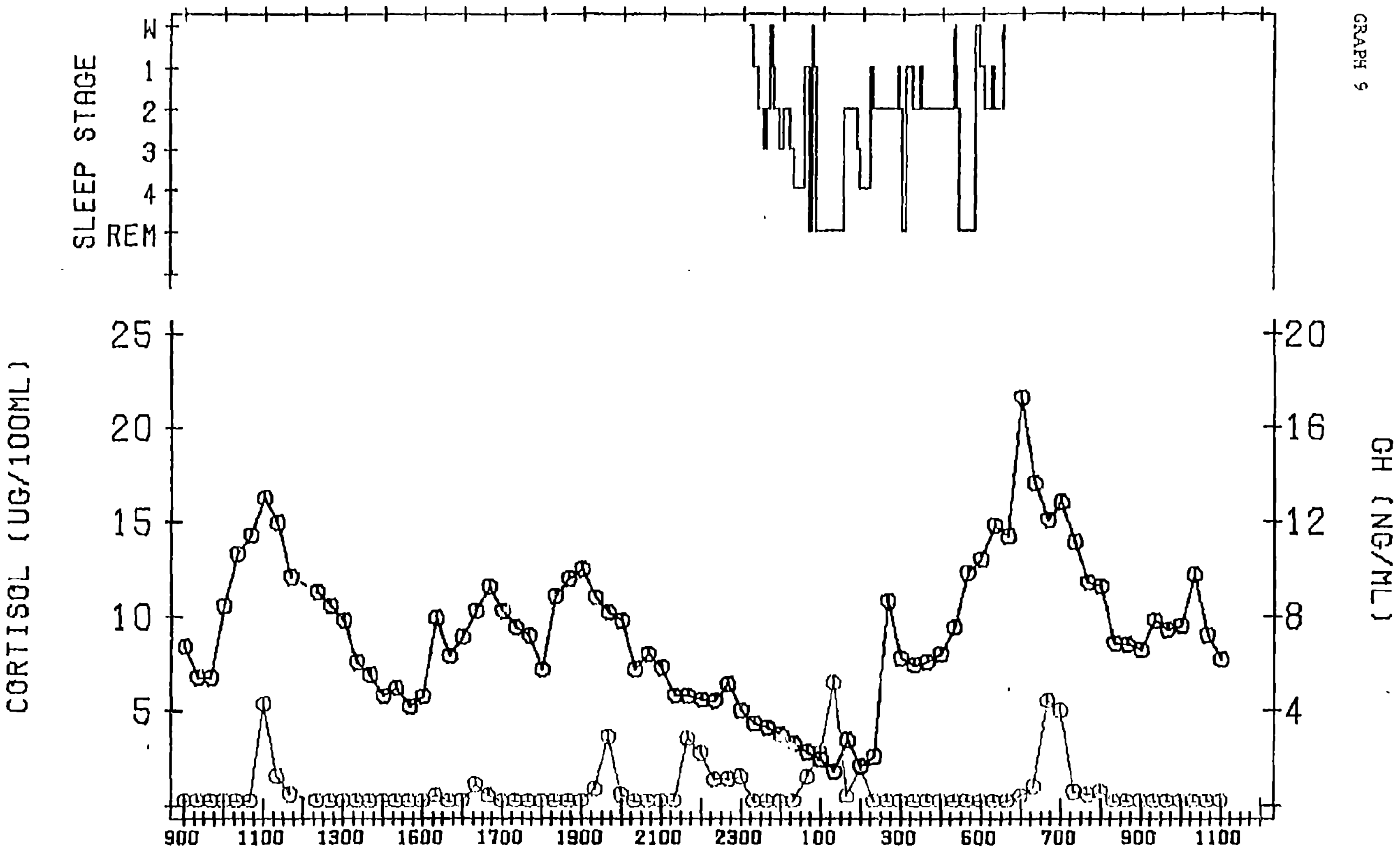

GRAPH 5
SLEEP STAGE
W
1
2
3
4
REM
CORTISOL (UG/100ML)
25
20
15
10
5
GH (NG/ML)
20
16
12
8
4
700
900
1100
1300
1500
1700
1900
2100
2300
100
300
500
700
900
MCINTOSH 5/8/75 END SHIFT
2252

GRAPH 7



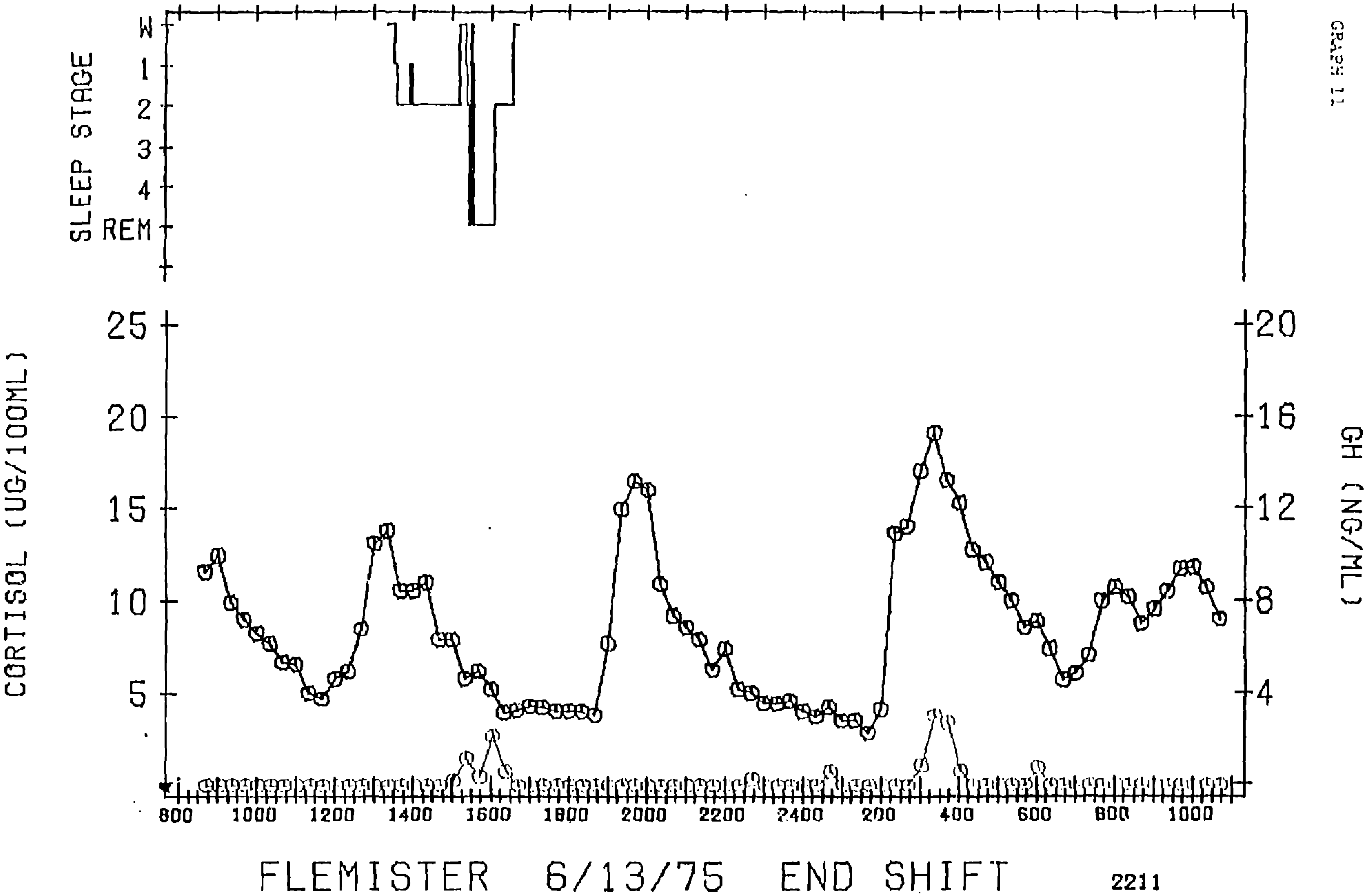
NORMAN 3/13/75 BEGIN SHIFT 2368

GRAPH 9

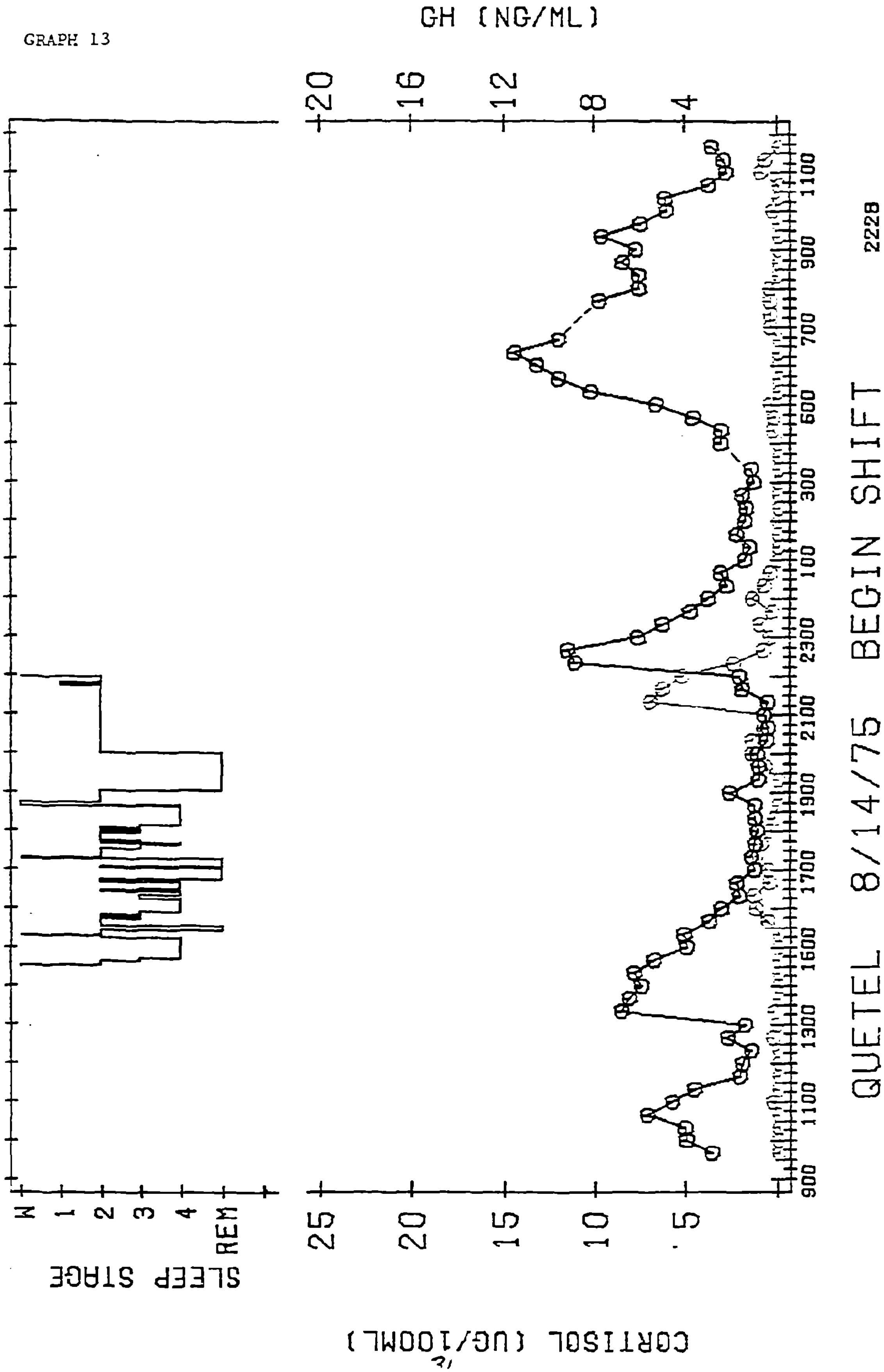


FLEMISTER 5/29/75 BASELINE 2204

GRAPH 11

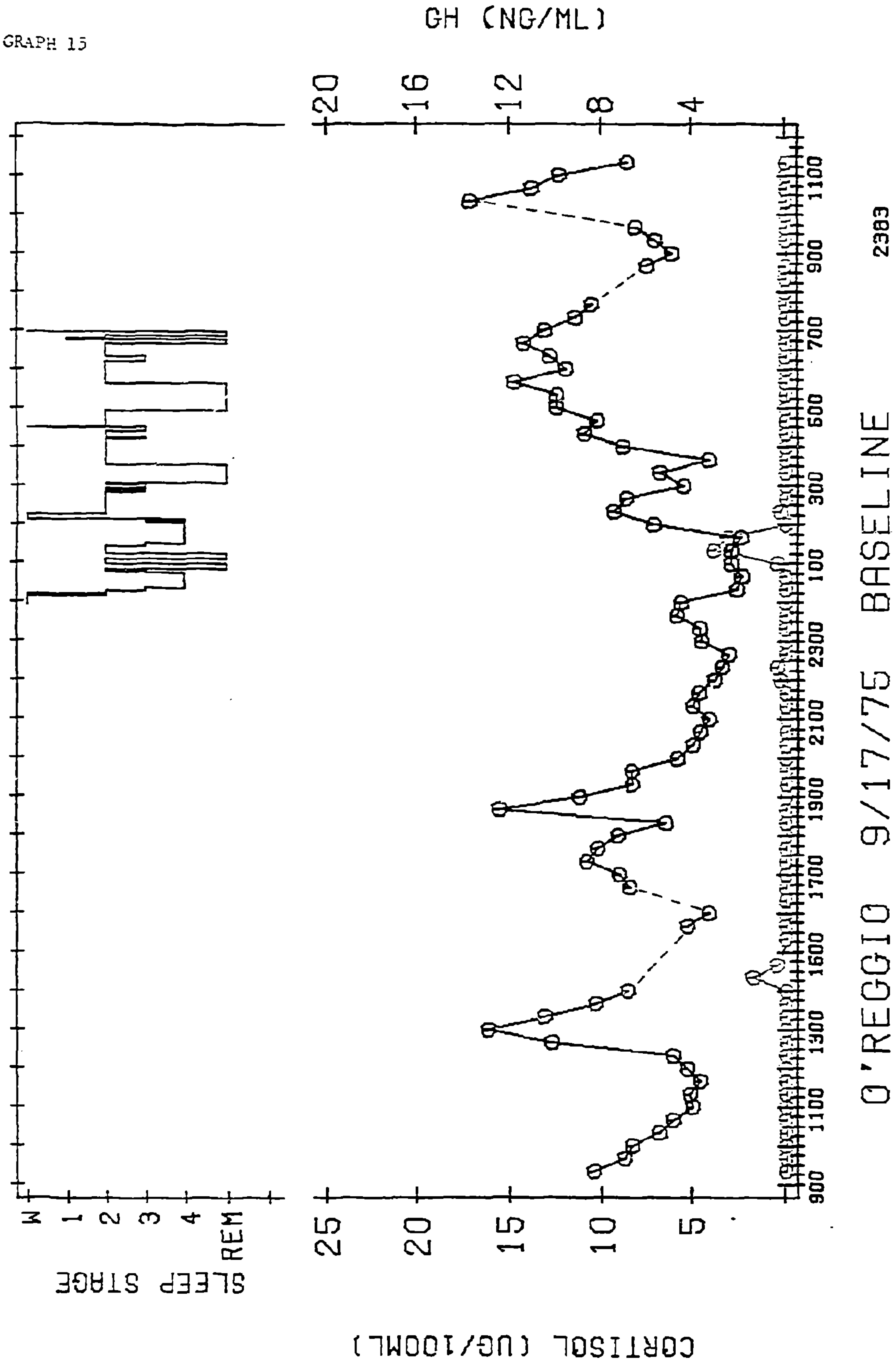

SLEEP STAGE
W
1
2
3
4
REM
CORTISOL (UG/100ML)
25
20
15
10
5
GH (NG/ML)
20
16
12
8
4
800
1000
1200
1400
1600
1800
2000
2200
2400
200
400
600
800
1000
FLEMISTER 6/13/75 END SHIFT
2211

GRAPH 13



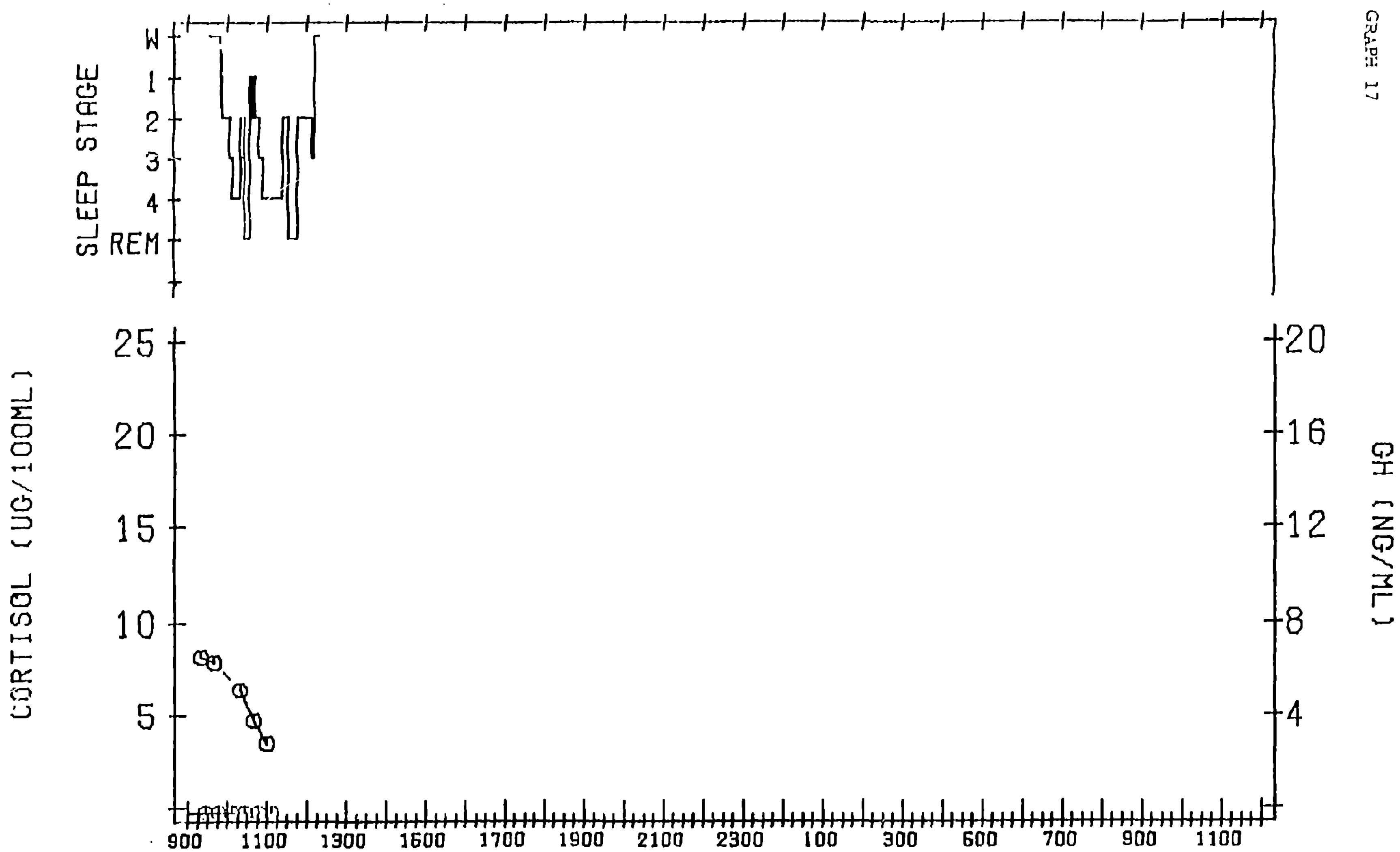
GH (NG/ML)
20
16
12
8
4
SLEEP STAGE
W
1
2
3
4
REM
CORTISOL (UG/100ML)
25
20
15
10
5
900
1100
1300
1500
1700
1900
2100
2300
100
300
500
700
900
1100
QUETEL 8/14/75 BEGIN SHIFT
2228

GRAPH 15



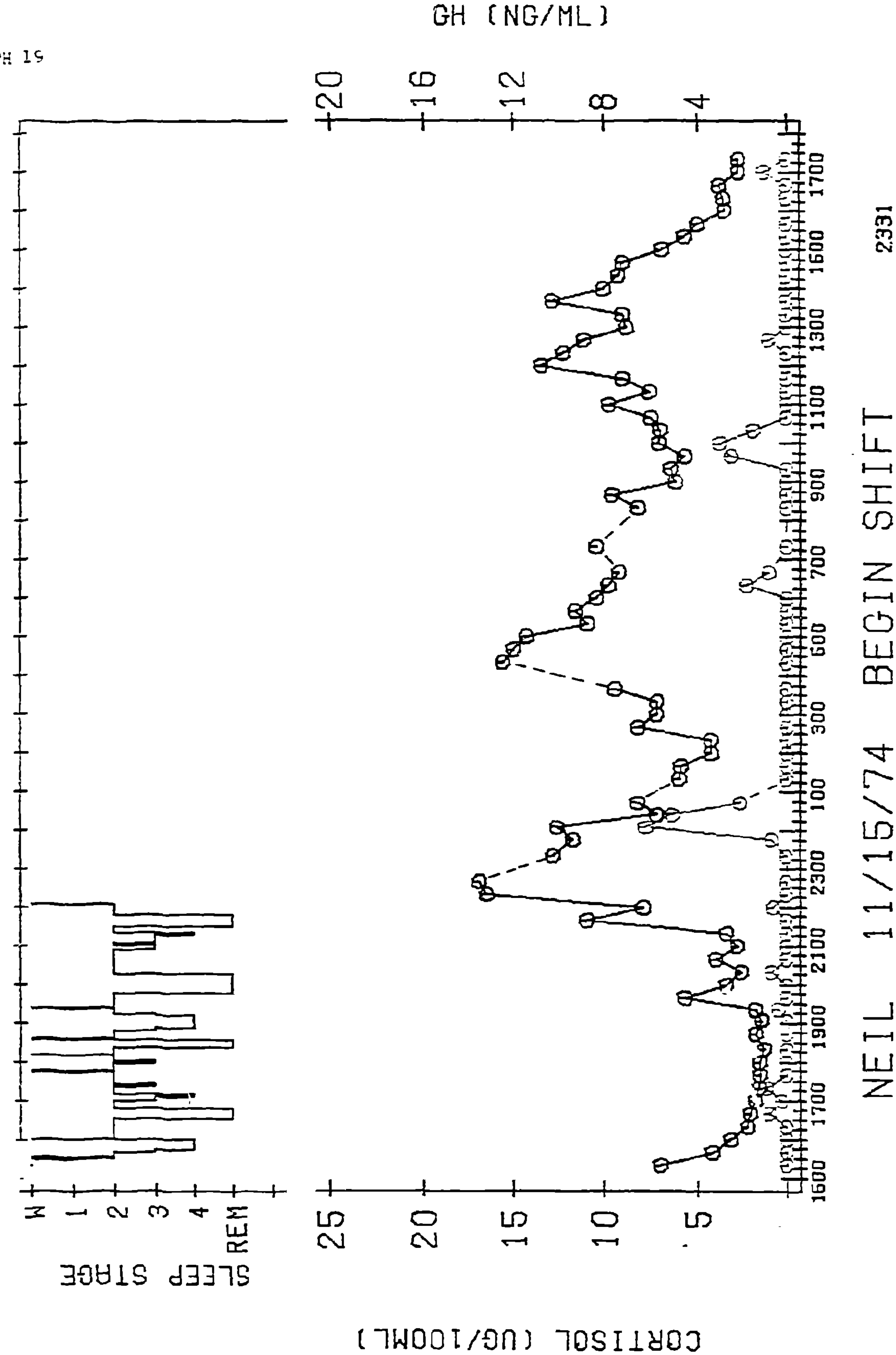
GH (NG/ML)
SLEEP STAGE
W
1
2
3
4
REM
CORTISOL (UG/100ML)
25
20
15
10
5
20
16
12
8
4
900
1100
1300
1500
1700
1900
2100
2300
100
300
500
700
900
1100
O'REGGIO 9/17/75 BASELINE
2383

GRAPH 17

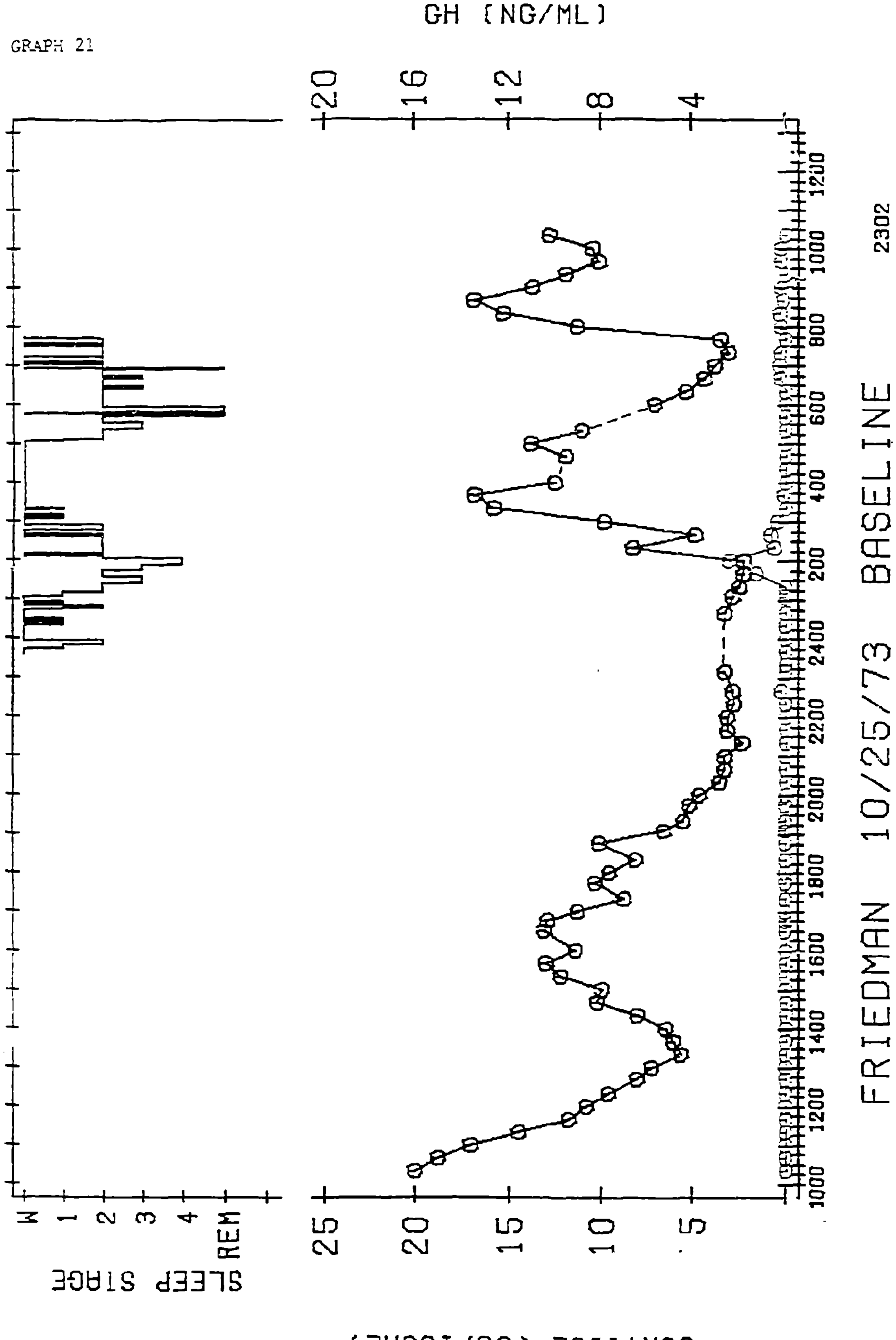


O'REGGIO 10/9/75 END SHIFT 2392

GRAPH 19

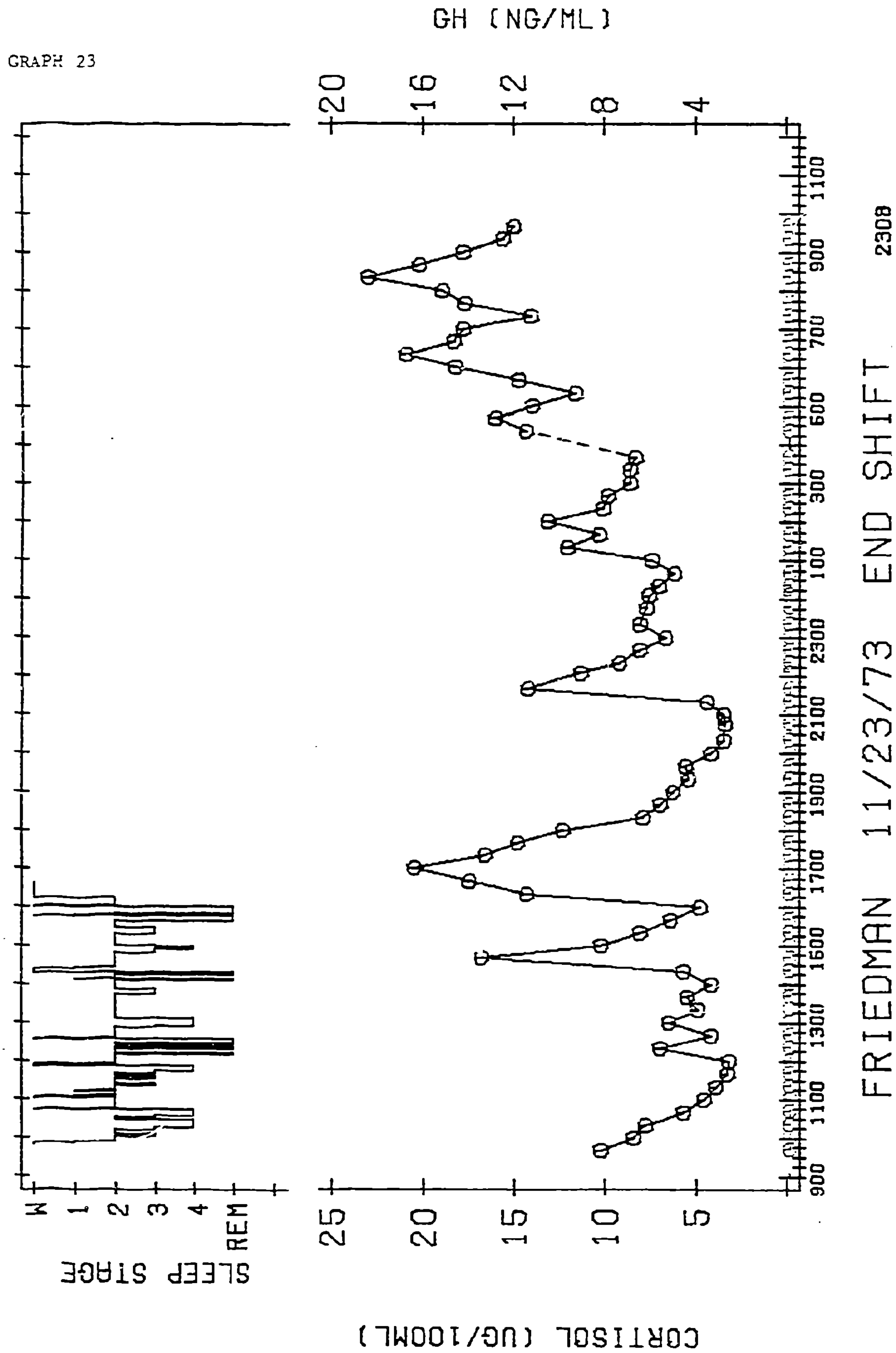

NEIL 11/15/74 BEGIN SHIFT
2331
SLEEP STAGE
W
1
2
3
4
REM
CORTISOL (UG/100ML)
GH (NG/ML)

GRAPH 21

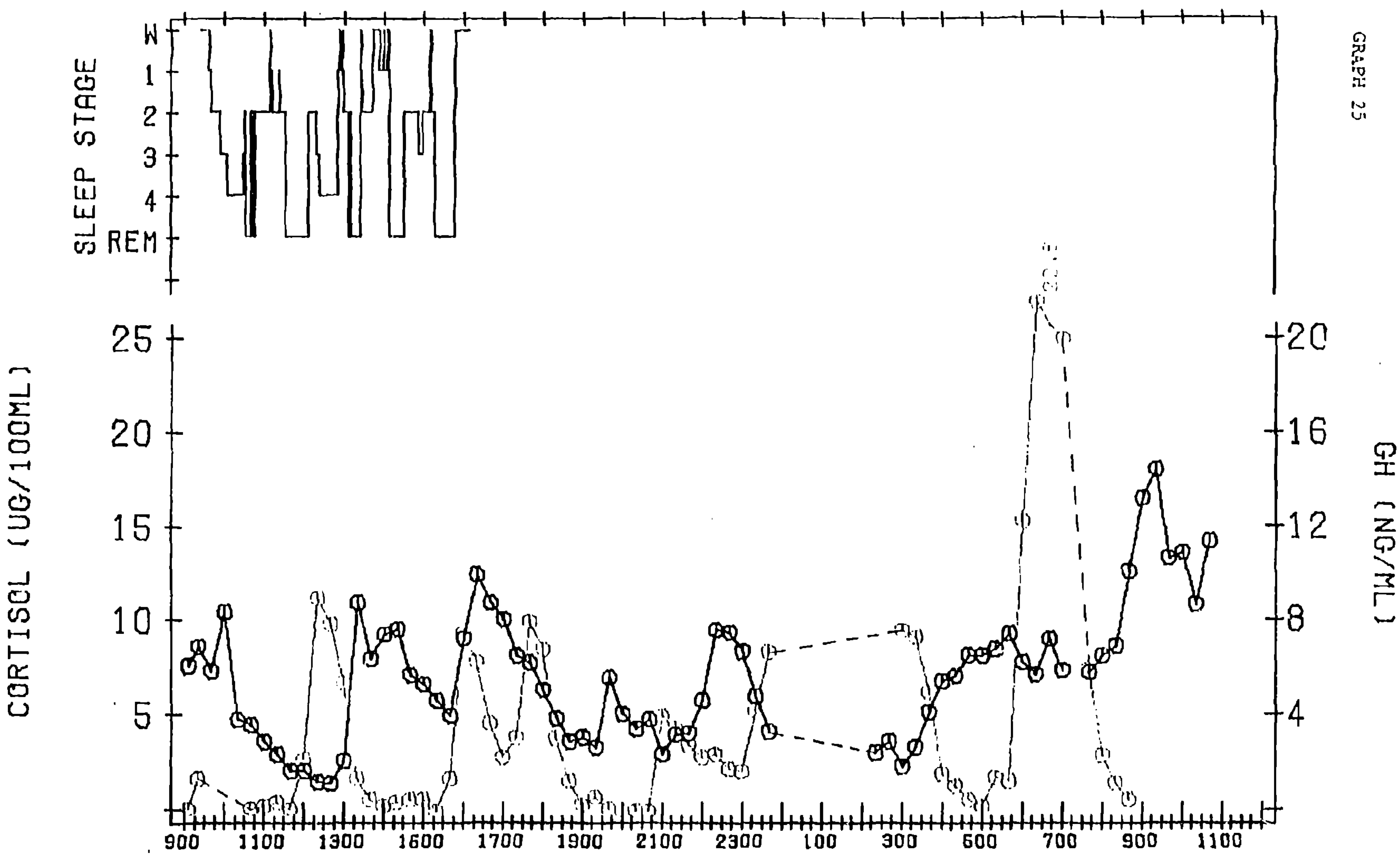


GH (NG/ML)
20
16
12
8
4
SLEEP STAGE
W
1
2
3
4
REM
CORTISOL (UG/100ML)
25
20
15
10
5
1000
1200
1400
1600
1800
2000
2200
2400
200
400
600
800
1000
1200
FRIEDMAN 10/25/73 BASELINE
2302

GRAPH 23

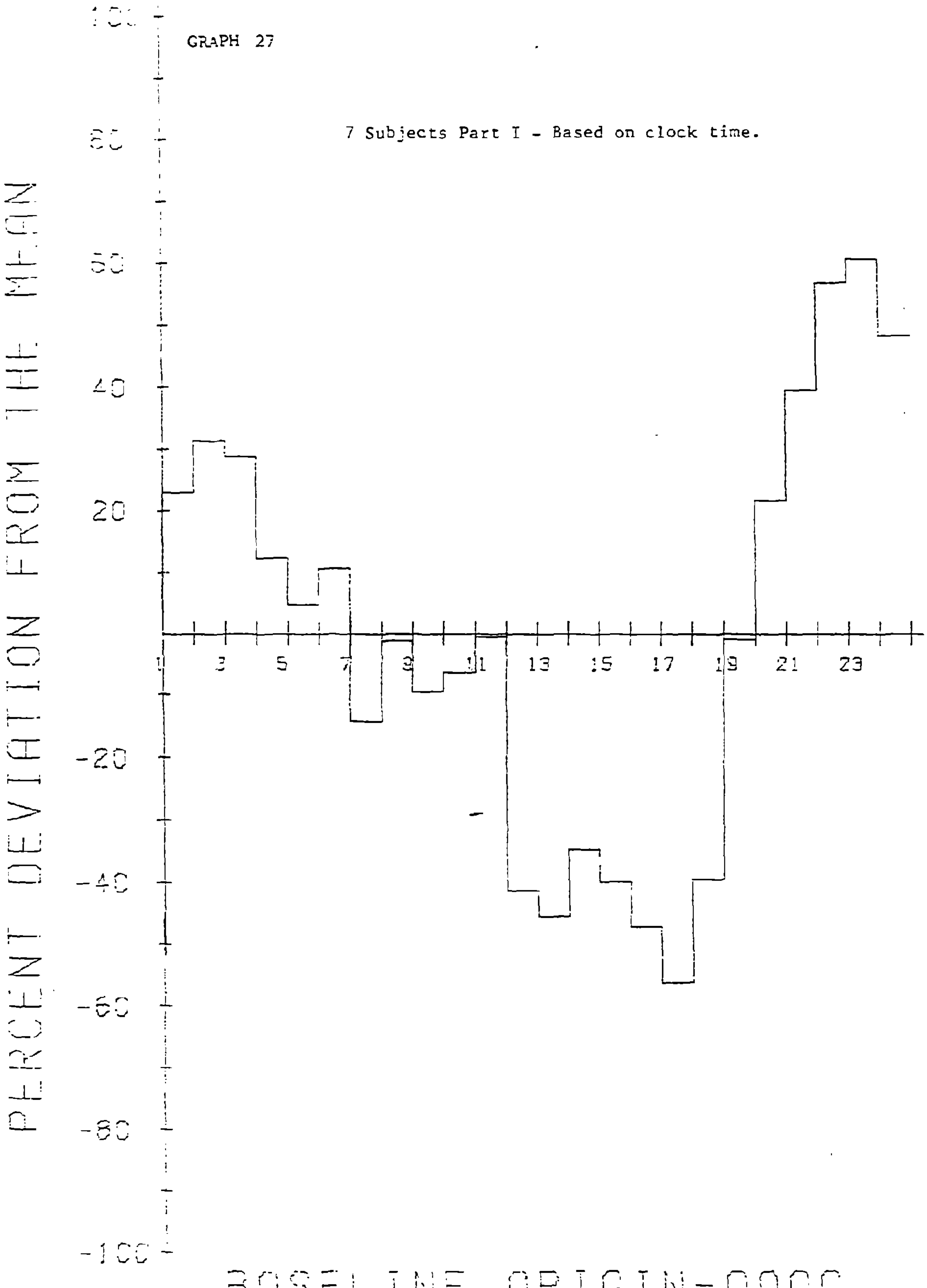

FRIEDMAN 11/23/73 END SHIFT
2308
GH (NG/ML)
CORTISOL (UG/100ML)
SLEEP STAGE
W
1
2
3
4
REM
25
20
15
10
5
20
16
12
8
4
900
1100
1300
1500
1700
1900
2100
2300
100
300
500
700
900
1100

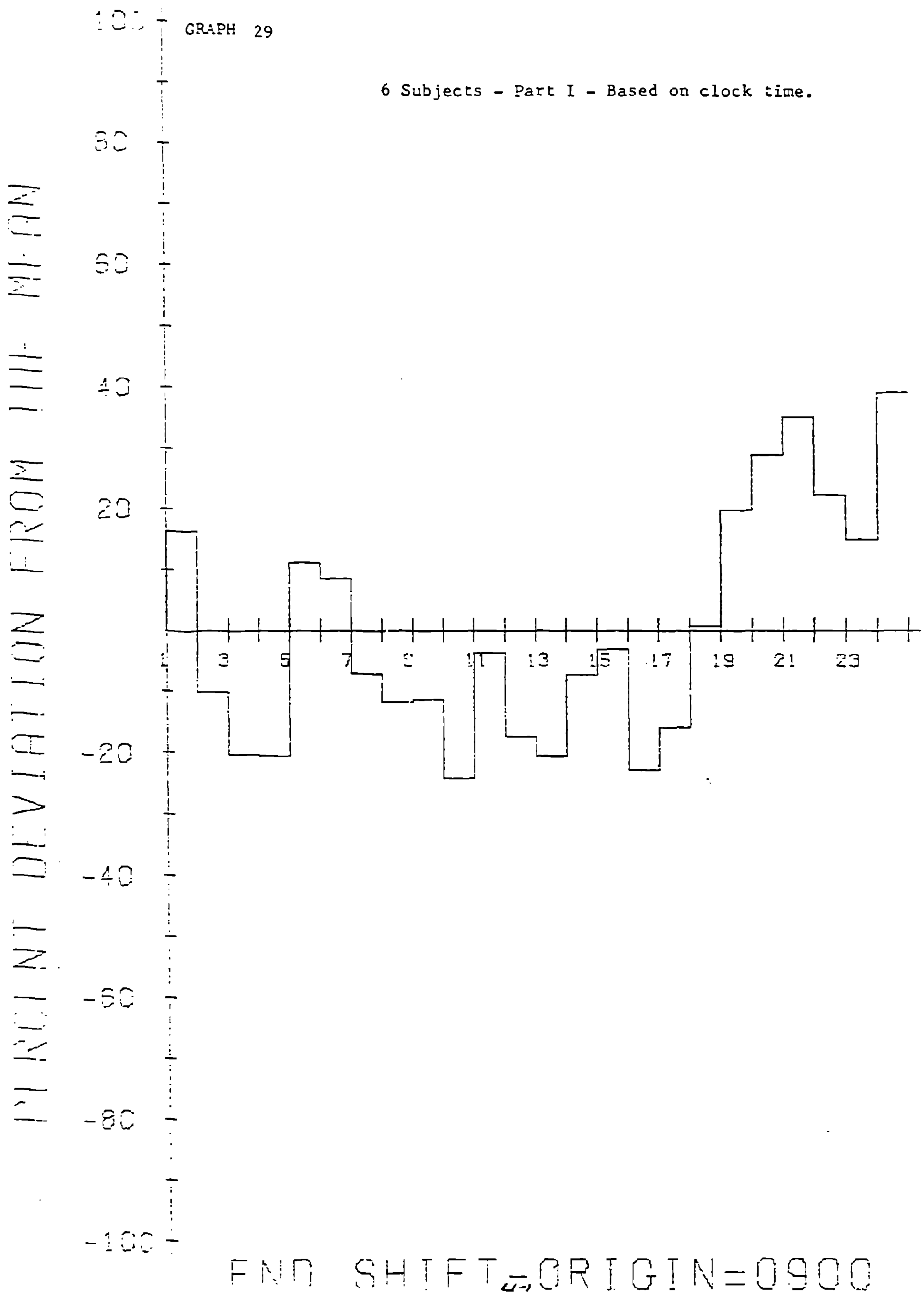
GRAPH 25



J. MIRANDA 1/26/75

2354


GRAPH 27
7 Subjects Part I - Based on clock time.
PERCENT DEVIATION FROM THE MEAN
100
80
60
40
20
-20
-40
-60
-80
-100
1
3
5
7
9
11
13
15
17
19
21
23
BASELINE-ORIGIN=0900


GRAPH 29
6 Subjects - Part I - Based on clock time.
PERCENT DEVIATION FROM THE MEAN
100
80
60
40
20
-20
-40
-60
-80
-100
1
3
5
7
9
11
13
15
17
19
21
23
END SHIFT ORIGIN=0900

GRAPH 31

6 Subjects - Part I - Based on sleep onset time.