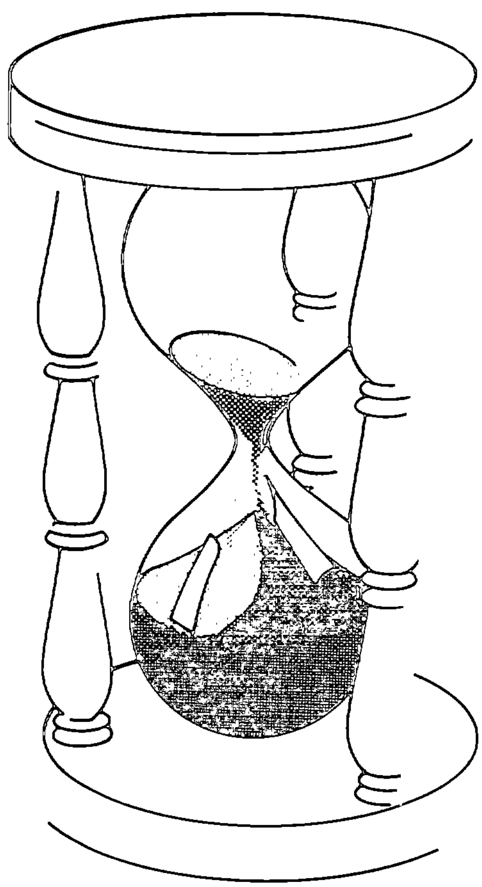
NIOSH

PHYSIOLOGICAL AND PSYCHOLOGICAL ASPECTS OF NIGHT AND SHIFT WORK



U. S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Public Health Service
Center for Disease Control
National Institute for Occupational Safety and Health

50272-101

REPORT DOCUMENTATION PAGE	1. REPORT NO.	2.	3. Recipient's Accession No. PB86 152972 /AS

4. Title and Subtitle
Physiological and Psychological Aspects of Night and Shift Work

5. Report Date
December 1977

6.

7. Author(s)

8. Performing Organization Rept. No.
78-113

9. Performing Organization Name and Address

NIOSH
4676 Columbia Parkway
Cincinnati, Ohio 45226

10. Project/Task/Work Unit No.

11. Contract(C) or Grant(G) No.
(C)
(G)

12. Sponsoring Organization Name and Address

NIOSH
4676 Columbia Parkway
Cincinnati, Ohio 45226

13. Type of Report & Period Covered

14.

15. Supplementary Notes

16. Abstract (Limit: 200 words)

In this review, the results of physiological and psychological studies related to night and shift work have been collected. They are discussed mainly from the standpoint of their possible utilization in industry, in understanding the problems of shift work, the sources of possible troubles and complaints connected with shift work, and in the alleviation of the problems.

The wide variety of jobs involving shiftwork in modern industry indicates the need for this review. In Chapter I and Addendum VI and VIII circadian rhythms in biological functions are reviewed with the purpose of drawing the reader's attention to the variations in the organism's functional capacities during day and night, and as a result of that, variations in responsiveness to environmental factors, as well as, to work. It is not the intention of the author to suggest that all night-day variations observed in physiological functions, sensory-motor performance, and work efficiency reflect only the circadian rhythm. The problems related to physical work are dealt with in Chapter II and Addendum VII, mental and sensory-motor performance in Chapter III, and some aspects of the night work in hot environments in Chapter IV. The main objective is to attempt an answer to the question: Is it appropriate to impose the same demands on a worker employed at night as those required of a worker during the day and, if not, to what degree and in what respect should the requirements be modified?

17. Document Analysis a. Descriptors
shift-work, circadian-rhythms, physiological-effects, psychological-effects

b. Identifiers/Open-Ended Terms

c. COSATI Field/Group

18. Availability Statement:	19. Security Class (This Report)	21. No. of Pages
AVAILABLE TO THE PUBLIC	Unclassified	91
	20. Security Class (This Page) Unclassified	**22. Price**

(See ANSI-Z39.18) *See Instructions on Reverse* OPTIONAL FORM 272 (4-77) (Formerly NTIS-35) Department of Commerce

PHYSIOLOGICAL AND PSYCHOLOGICAL ASPECTS OF NIGHT AND SHIFT WORK

Jadwiga Wojtczak-Jaroszowa, M.D.

Institute of Food and Nutrition
Warsaw, Poland

U.S. DEPARTMENT OF HEALTH, EDUCATION, AND WELFARE
Public Health Service
Center for Disease Control
National Institute for Occupational Safety and Health
Cincinnati, Ohio

December, 1977

i.a

DHEW (NIOSH) Publication No. 78-113

Library of Congress No. 77-600069

PREFACE

This monograph was prepared by Dr. Wojtczak-Jaroszowa at the National Institute for Occupational Medicine in the Textile and Chemical Industries, Lodz, Poland, and the Food and Nutrition Institute, Warsaw, Poland; under the auspices of a Polish-American Program (agreement number 05-516-1.16) financed by the National Library of Medicine, Bethesda, Maryland, USA.

The National Library of Medicine gave the National Institute for Occupational Safety and Health permission to publish this monograph in the NIOSH Technical Report Series. In preparing the manuscript for publication, some editorial rewriting was done to make the text conform with standard English sentence construction and word usage. However, special effort was made not to alter the factual material, the intent, and the conclusions of the author.

During the past year, since the original text of the monograph was prepared, new research data with extensive references have been made available which warranted their inclusion in this monograph. The material was added as a three-section Addendum. Figures and references in the Addendum are identified and listed independently from those in the main body of the monograph.

Austin Henschel, Ph.D.
Editor

CONTENTS

ACKNOWLEDGMENTS

The editor expresses his thanks and appreciation to Joe Bobbey, Carolyn Browning, and Gail Lutter for their assistance in preparing the manuscript for the printers, to A. Lauman for advice and assistance in the preparation of the figures, and to Lorice Ede for her advice and guidance.

Permission of the authors and publishers to reproduce figures is gratefully acknowledged. Specific reference, as appropriate in the text, is made for each figure reproduced.

INTRODUCTION

The necessity for night and shift work* originates not only from economic factors, but from social conditions as well. Night and shift work are encountered commonly in public services such as transport, army, police, telecommunications, and health care and in those branches of industry where continuity of operations, whether for technological or economic reasons, is indispensable, e.g., in electrical plants, gas works, oil refineries, glass factories, printing houses, coal mines, electrochemical industry, pharmaceutical plants, and metal smelting industries.

Often an interruption of a continuous technological process, even if only for a few hours, would cause disproportionately increased costs. An additional reason for introducing shift work systems, is the need for maximal use of expensive machinery, as well as, for production needs. Progress in automation of technological processes and the wide use of computers have also stimulated the introduction of shift work.

In recent years, numerous international symposia and meetings have been devoted to problems related to shift work. This growing preoccupation with the subject by physiologists, psychologists, industrial physicians, industrial engineers, sociologists, and economists results from the conflict arising between economic demands for greater numbers of workers on shift work on the one hand, and the stresses of shift work on those workers on the other. The necessity for applying the shift system in contemporary industry has stimulated research studies with goals to decrease the stressfulness of shift work, particularly the night shift.

In this review, the results of physiological and psychological studies related to night and shift work have been collected. They are discussed mainly from the standpoint of their possible utilization in industry, in understanding the problems of shift work, the sources of possible troubles and complaints connected with shift work, and in the alleviation of the problems.

The wide variety of jobs involving shift work in modern industry indicates the need for this review. In Chapter I, and Addendum VI and VIII circadian rhythms in biological functions are reviewed with the purpose of drawing the reader's attention to the variations in the organism's functional capacities during day and night, and as a result of that, variations in responsiveness to environmental factors, as well as, to work. It is not the intention of the author to suggest that all night-day variations observed in physiological functions, sensory-motor performance, and work efficiency reflect only the circadian rhythm. The problems related to physical work are dealt with in Chapter II and Addendum VII, mental and sensory-motor performance in Chapter III, and some aspects of the night work in hot environments in Chapter IV. The main objective is to attempt an answer to the question: Is it appropriate to impose the same demands on a worker employed at night as those required of a worker during the day and, if not, to what degree and in what respect should the requirements be modified?

Special attention is paid in Chapter V to the importance of sleep after night duty. In Chapter VI, data are presented on various arrangements of shift systems, as well as, on organization of the working time and breaks during the night shift.

It should be noted that studying shift workers under conditions of their normal occupational activities does not permit an estimation of the extent that the observed variations result from the endogenous circadian rhythm and to what degree they reflect the influence of the exogenous "synchronizing" factors. In this review, the results of research studies are presented in a descriptive manner without always going into causes of the observed variations, whether they were the consequence of the endogenous circadian rhythm or of exogenous factors.

---

* Definition of the term "shift work" denotes an employment system in which the working hours of the worker change periodically, but more or less regularly. Thus, for example, a two-shift system includes most commonly a morning and an afternoon shift; the three shift system, in addition, includes a night shift. This review deals mainly with systems of three or more shifts, one of which is a night shift.

CHAPTER I

CIRCADIAN* RHYTHM OF BIOLOGICAL FUNCTIONS AND NIGHT WORK

"Biological cycles exert their power upon us from birth until we die, although most of us take little note of them, remaining ignorant of regular periodicities in our moods, strength, days of efficiency, days of sluggishness"

— *G. G. Luce, J. Segal, 1966*

CIRCADIAN PERIODICITY

Most physiological functions and metabolic changes display a circadian periodicity with a cycle of about 24 hours duration (7,19,44,204). There are many studies concerning the circadian rhythms of body temperature, heart rate, blood pressure, urine production, blood leucocytes (20,109,132,139,140,180), secretion of enzymes and hormones, excretion of electrolytes in the urine (6,39,75,120,146,175,187,233,237, 289), rate of dentin calcification (184), and metabolic activity of bone tissue (232). Day-night variations in physical, mental, and sensory-motor performance also have been observed (13,54,87, 89,90,98,115,152,172,236,262).

Rhythms of many functions are interrelated; however, this does not mean that their maxima or minima coincide in time. Thus, for instance, elevation of skin temperature of the extremities in the evening is accompanied by a decrease of the deep body temperature (8). Urinary excretion of electrolytes shows circadian variations (65,77); however, the peak of magnesium and calcium excretion coincides with the diurnal minimum for chlorides (figs. 1a, b). Adrenalin and noradrenalin secretion is higher during the day than at night, whereas the concentration of antidiuretic hormone peaks at night (73,84,154,239). According to observations by Doe, et al. (64,65), the maximum sodium and potassium excretions are in phase with 17-OHCS in urine (fig. 2a). In

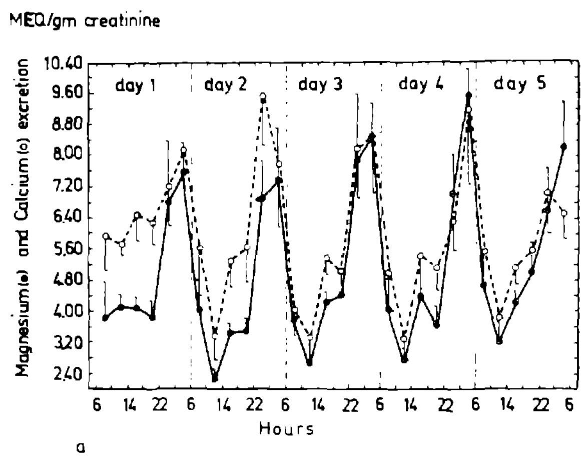


Figure 1a. Circadian excretion cycles of magnesium and calcium for 8 subjects (age 6 to 17 years) who were examined for 120 hours on a standard dietary regimen ingested every 4 hours (Fiorica et al., 1968).

material by Bartter et al. (24), the peak of these electrolytes occurred about six hours prior to the maximal level of 17-OHCS and aldosterone in urine (fig. 2b). The peak and trough of the blood eosinophils appear at the time of minimal and

---

* The term "circadian rhythm" is derived from Latin "circa dies" which means approximately 24-hour periods. The term is used more frequently than "24-hour biological rhythm" because it was shown that in artificial conditions of isolation from environmental stimuli, some rhythms do not adhere strictly to a 24-hour periodicity (10, 12, 45, 95, 186).

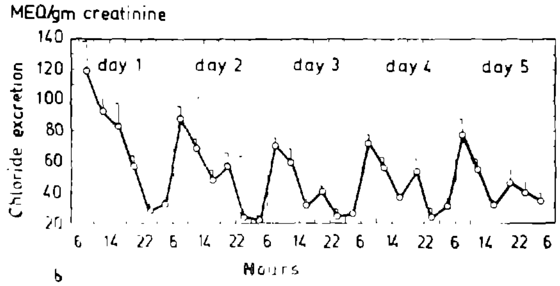


Figure 1b. Circadian excretion cycles of chloride for 8 subjects (age 10 to 17 years) who were on a standard dietary regimen (Fiorica et al., 1968).

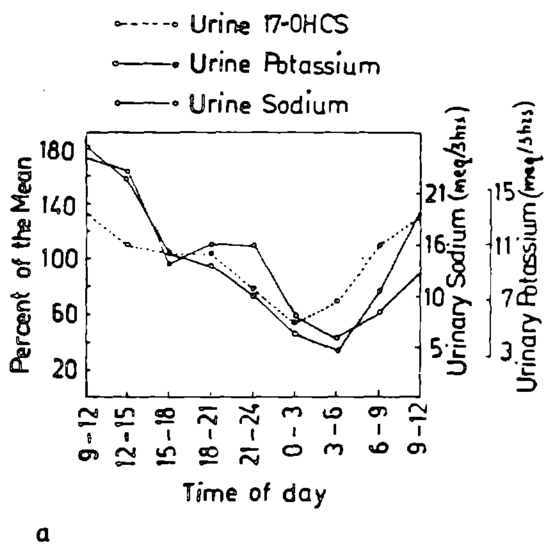


Figure 2a. Relationship of mean diurnal variation in excretion of sodium, potassium, and 17-OHCS in 8 normal subjects. The lowest electrolytes excretion occurred in the 3-hour period following the lowest excretion of 17-OHCS (Doe, Vennes, and Flink, 1960).

maximal 17-KS urinary excretion, respectively (fig. 3). In turn, the peak of eosinophils and lymphocytes in peripheral blood coincides with the trough of body temperature. On the other hand, the curve of body temperature reaches the diurnal peak together with the urinary excretion of 17-OHCS (fig. 4). The maxima and minima of the different types of circulating blood leucocytes are also manifested at different times of the day.

Circadian periodicity of biological functions determines the variations in susceptibility of the organism to different environmental factors. Time related responses to many drugs and pathogenic agents are discussed by many authors

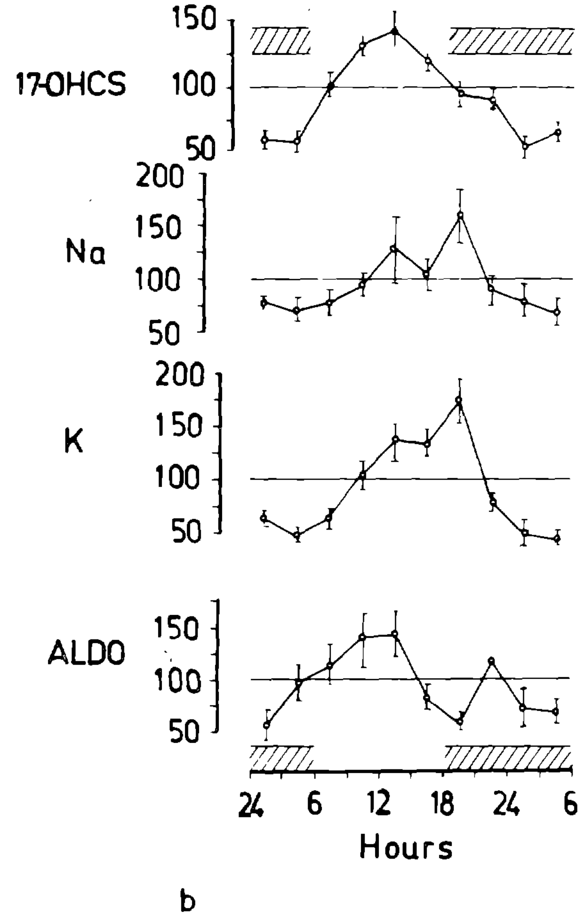


Figure 2b. Relative change in excretion of steroids, sodium, and potassium in a group of seven college girls (Bartter, Delea, and Halberg, 1962).

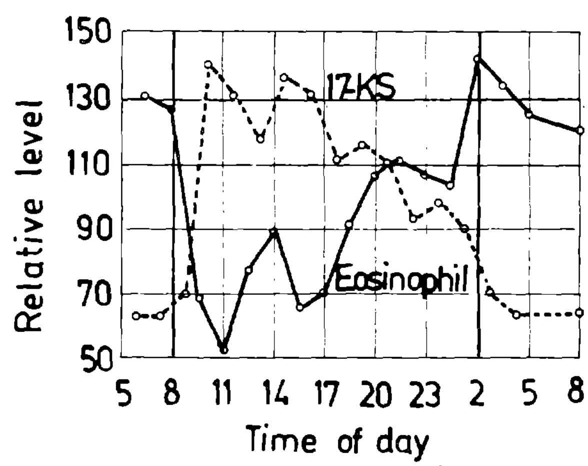


Figure 3. Circadian rhythms of circulating eosinophils and of excretion of 17-KS in a group of 17 healthy males (Halberg, 1953).

(108,112,125,165,176,210,214,242,237). Circadian rhythm of the time of human death from

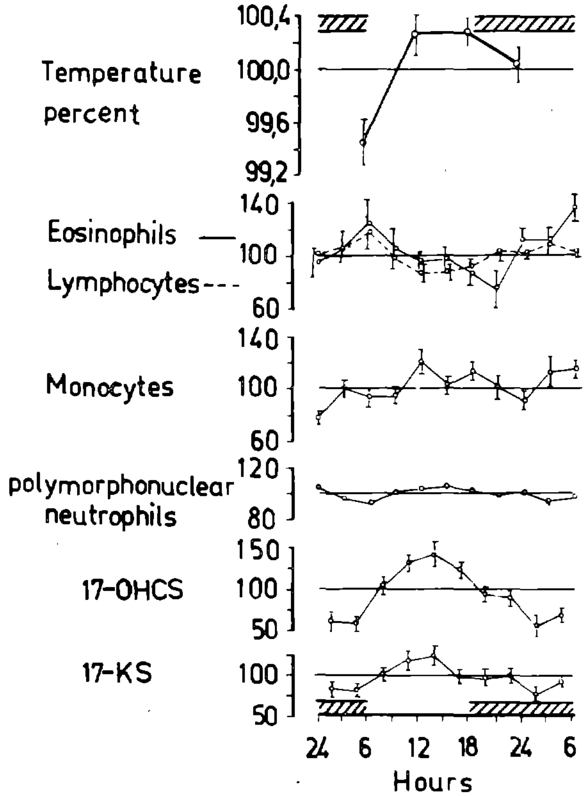


Figure 4. Relative changes in body temperature, circulating leucocytes, and urinary steroids in seven college girls (Bartter, Delea, and Halberg, 1962).

some diseases has been described (235). In the course of many diseases, the symptoms are usually more severe at particular times of the day or night. There is no exaggeration in the statement of Luce and Segal that "a man at 10 a.m. is not the same man at 4 p.m. or midnight. Indeed, the same individual is radically different at 2 a.m." (165). Even the responsiveness to the administration of salicylate varies with the time of day (fig. 5); this is often not appreciated in spite of the common every day use of salicylates (215).

The circadian rhythms of a number of physiological functions persist even under controlled conditions with an artificial lighting regimen, in which the local time scale and social schedule are abolished. The persistence of many rhythms does not seem to depend upon changes in motor activity and environmental factors, because they also can be observed in subjects resting continuously for 24 hours, as well as, in people living under artificial conditions of isolation (11,45,69,186,188). Similarly, the rhythms are maintained during starvation or low-calorie food intake, restriction of fluids and mineral salts, and under conditions of sleep deprivation (82,83,85,

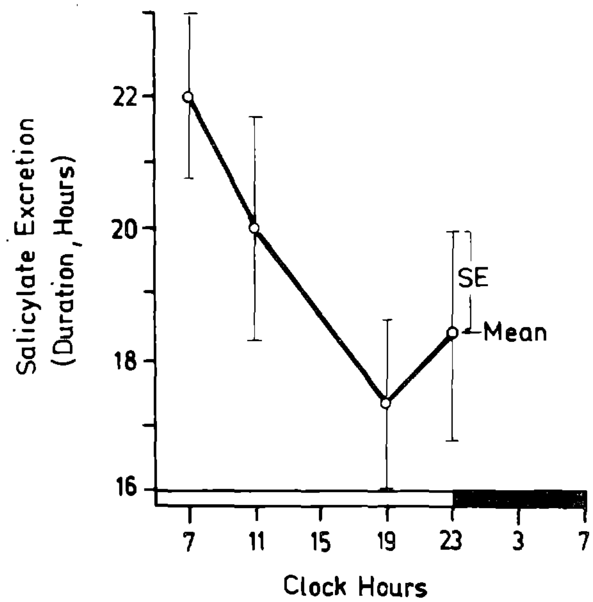


Figure 5. Circadian variation in salicylate excretion. The medicine was given orally at 7 a.m., 11 a.m., 7 p.m., or 11 p.m. (Reinberg et al., 1967).

154,210,212,213).

The periodicity which is maintained independently of the environmental conditions (as when the surrounding is artifically kept constant) is called the endogenous periodicity, in contrast with the exogenous rhythm whose phases can be related to changes in environmental factors. However, this classification is, at least with regard to some of the biological rhythms, of limited value in understanding their mechanisms. With several rhythms it is still a matter of dispute into which category they should be included. There is also the basic question of how long should a period of isolation last to be sufficient for assigning a given rhythm to the endogenous or exogenous category. The alteration of phases in time as a consequence of changes in the environment does not, however, mean that the given periodicity is of exogenous origin. It may just point to a synchronization of circadian periodicity with the environmental factors.

Many observations indicate a role of the hypothalamo-hypophyseo-adrenocortical system in the maintenance of circadian periodicity (4,54,70,76,105,131,149,242). This is understandable because this system plays a key role in physiological regulation, and because a large part of known hypophyseal hormones are the trophic ones, i.e., stimulating secretion of the other endocrine glands. On the other hand, the secretory function of the hypophysis remains under the control of the hypothalamus. Thus, for instance, a relationship exists between circadian variations of hypophyseo-adrenocortical activity and circulating leucocytes in blood. Halberg (107) has shown that the rhythm of blood eosinophils disappears after adrenalectomy. However, it was possible to restore this rhythm by administration of 11,17-oxycorticoids. Some rhythms (e.g., 17-OHCS secretion) are disturbed or abolished in patients with the Cushing's syndrome (64,65).

The phase relationship between the circadian pattern of urinary potassium and that of 17-OHCS, as well as, of aldosterone secretion, has been shown. This is understandable because the changes in potassium excretion depend on the action of the steroids. The variations in sodium excretion closely parallel those of potassium excretion (64,65,110,235). This would suggest (24) that besides steroids, sodium excretion is also controlled by other mechanisms; it is known that the influence of these hormones on the excretion of sodium and potassium is opposite. In Addison's disease, a decreased amplitude of circadian variations in sodium and potassium urinary excretion was noted (24). An experimental study performed on rats showed (210) that circadian variations in metabolism of some drugs in the liver are abolished by adrenalectomy whereas, they were maintained during starvation.

Some role in maintenance of circadian variations is attributed to visual stimuli, especially in lower animals (38,44,78,119,131,137). It was shown that the circadian rhythm of pineal gland function is related to the changes in light intensity: In many lower animals (e.g., fish and lizards), the pineal gland is a receptor of visual stimuli.* In rats, activity of the pineal enzyme, catalyzing the terminal stage of melatonin synthesis, is reduced under the influence of light. In some reptiles, amphibia, and fishes, the secretion of the melanophoric hypophyseal hormone is also regulated by visual stimuli. Both of these hormones, the melatonin secreted by the pineal gland and the melanophoric hormone of the hypophysis, may modify the color of the skin of reptiles and amphibia by changing the distribution of color granules in the melanocytes. It was observed that a constant night coloration of the skin was maintained in lizards after hypophysectomy.

The importance of the light-dark schedule for maintenance, of some circadian rhythms in humans is pointed out by observations made on blind people (118,123). Januszewicz and Wocial (123) noted that no day-night variations were found in urinary excretion of catecholamines in blind subjects, in contrast to people with normal vision. On the other hand, circadian periodicity of 17-OHCS secretion was maintained in the blind subjects, though the amplitude of the variations was lower (185). There is little doubt that visual stimuli play a special role in the adaptation of the organism to the alternating environmental factors. In lower animals, changes in the ambient temperature can exert an influence on some periodicities.

The fact that circadian periodicities occur even at the cellular level suggests that they must be linked to the cellular structural organization. It also implies an existence of a hypothetical "clock" of endogenous biological rhythms (9,38,68,108). A significant role in the timing of biological processes is attributed to the recycling of the mechanism regulating the transcription of template RNA from DNA (54,68). The self-sustaining endogenous cellular "clocks" are susceptible to environmental factors in such a way that they synchronize the metabolic cellular rhythm with external cyclic changes in the environment. In higher animals, this cellular timing is subjected to the overlying endogenous oscillatory "clock," localized in the central nervous system, which receives stimuli from the outside world and synchronizes the rhythms of particular biological functions. The basic role of the physiological organization of circadian changes is attributed to neural and neurohormonal regulation.

Finally, the biological circadian rhythm is considered a genetically determined phenomenon which enables the adaptation of the organism to normal variations of the environment connected with astronomical timing, signalized by exogenous synchronizers* (light-dark regimen, changes in ambient temperature, conditions of social life, meal schedules, etc.). In this way, factors determine only the position of the phases of endogenous rhythms. In ontogenesis the endogenous circadian periodicity has been synchronized with environmental changes, and we "learn" to sleep at night and to lead an active life

---

* In the course of ontogenesis, part of the pineal gland of some lower vertebrates evolves into an organ of vision; the so called third eye.

* The factors playing a role of synchronizers are called the "timegivers" (Zeitgebers) in German literature (Aschoff, 1958).

in the daytime. In this sense, the biological rhythms are the result of the interaction of internal and external timing.

EFFECT OF NIGHT WORK ON CIRCADIAN RHYTHMS

Night work is connected with the necessity of inverting the normal sleep-wake cycle. Under artificial circumstances of isolation with altered day-night regimen, after time zone translocation, or in industrial situations where undisturbed day sleep is possible, some changes in bodily rhythms corresponding to the actual sleep-wake schedule occur (51, 52, 93, 134, 136, 139, 141, 150, 159, 162, 163, 195, 198, 206, 225, 238, 250). Such adaptation is observed especially in situations in which all members of a given social group keep the same diurnal rest-work pattern. For instance, in the course of long distance flights with time zone translocation, Klein, Wegmann, and Hunt (136) observed some changes in circadian periodicity of body temperature (fig. 6). Colquhoun, Blake, and Edwards (47,48) noted the changes in the pattern of body temperature in subjects employed in a simulated shift system, in which the hours of night duty and day sleep were kept constant for about 2 weeks (fig. 7).

For shift workers who live under usual housing conditions, have families, and want some active social life, the situation is entirely different. The friends, family, and neighbors to whom the workers return every day after night duty, lead normal lives. They are active at the time the shift worker tries to sleep. Irrespective of work at night, the normal diurnal pattern of body temperature is usually sustained. During the night shift, the body temperature is higher at the beginning of the shift and it falls gradually during the night, regardless of the worker's physical activities. On the other hand, during sleep in the day hours, the body temperature is usually higher than during the night work.

In the shift workers studied by van Loon (255), body temperature rose only slightly during the night shift in spite of being on the night shift for weeks, but it still remained lower than during the day shifts (fig. 8). Similarly, Migeon et al. (185), found normal circadian rhythms in circulating eosinophils, as well as, in iron and 17-OHCS concentration in the plasma of subjects (nurses and watchmen) who worked continuously on the night shift for at least 6 months (fig. 9).

In our own investigation (201,283,284), cotton mill workers with long experience with a shift work system were studied. In all workers, the body temperature was higher during the day shifts than during the night. These differences were statistically significant for 80 percent of workers (fig. 10a). The systolic blood pressure was also lower during the night shift (fig. 10b) and the differences in heart rate were less pronounced (fig. 10c). It was characteristic that the same pattern of the physiological curves was shown on each day of the week for a given shift. This was especially evident in the curves of body temperature (figs. 11a, b, c). Thus, during the week of night shift work the lowest values were always noted at about 2 a.m. on the first, as well as, on the last night of the week (the slight rising trend of these values over the week was statistically insignificant). According to Gambashidze (87,89), the gradual fall of body temperature in shift workers (subway employees and bakers) was observed during a week on the night shift. The author suggests that this was an effect of fatigue connected with insufficient sleep during the period of night shift work.

Total inversion of circadian rhythms is not often observed in shift workers. In several cases, however, some flattening of diurnal curves or diminution of the differences in values of physiological functions between measurements performed on day and night shifts are observed (84,110,201,246,255). However, the return to a normal diurnal periodicity usually occurs faster, commonly within the first day back on a normal activity schedule. There are some suggestions that the character of the work performed by shift workers exerts an essential influence on the course of the changes in circadian rhythms. Namely, the inversion of some rhythms is more frequently observed when the work requires muscular activity than during mental or monotonous work (21, 181, 246). According to Barhad and Pafnote (22), the character of work has as much influence on the adaptation to night work as the influence of the shift system itself.

The length of period sufficient for the inversion of circadian rhythm due to inversion of the sleep-wake cycle, varies for different physiological functions (84,159,186,271). Gambashidze (89) suggested that phylogenetically "younger" systems adapt more readily to an inversion of the sleep-wake cycle than do phylogenetically "older" ones.

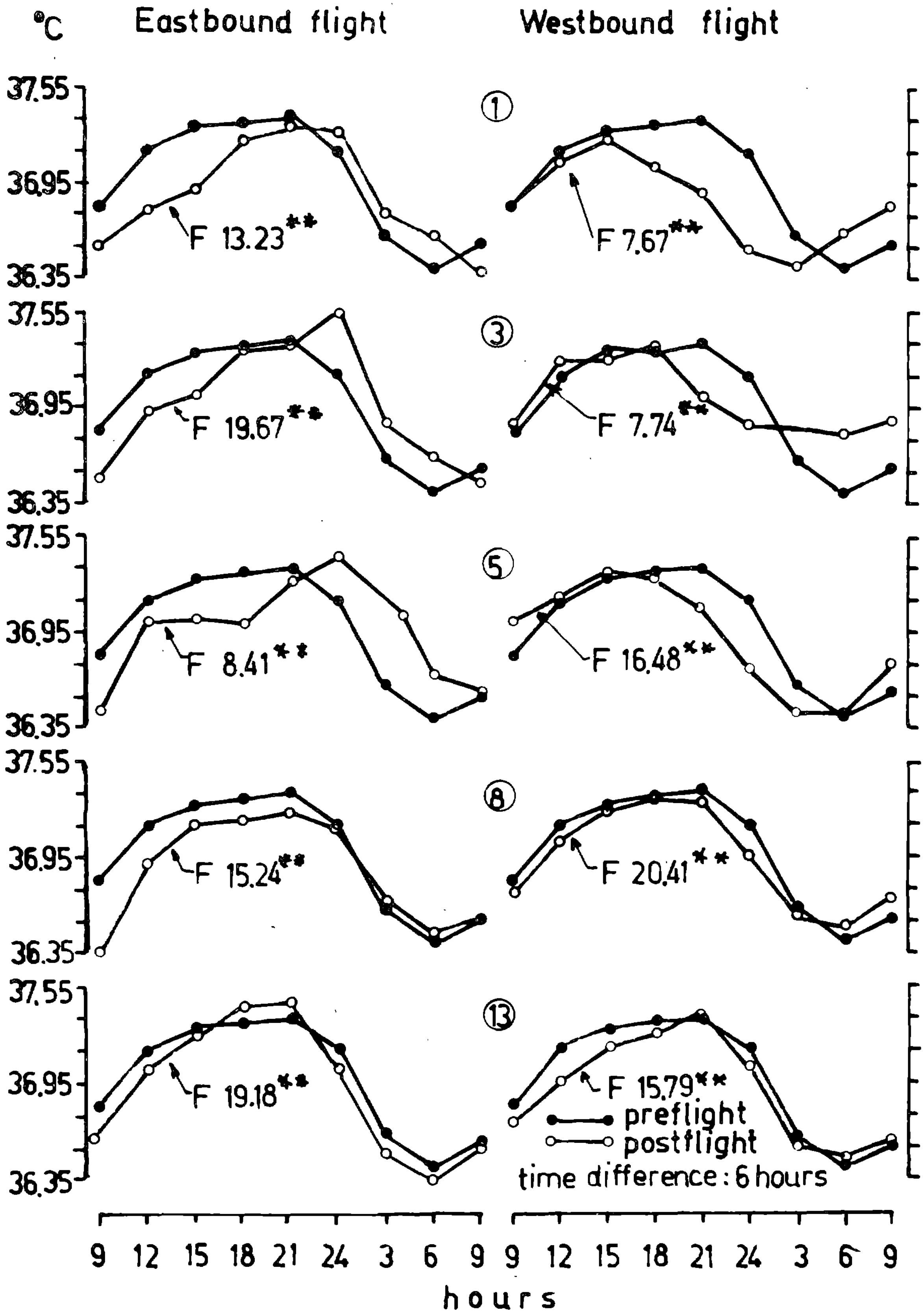


Figure 6. The effect of transmeridian flights on rectal temperature (average, N = 8, F-ratio for "time of day" variation: p < 0.001). Measurements were performed nine times throughout the day at 3-hour intervals for 3 days before the outgoing flight and on days 1, 3, 5, 8, and 13 following the flights in each direction (Klein, Wegmann, and Hunt, 1972).

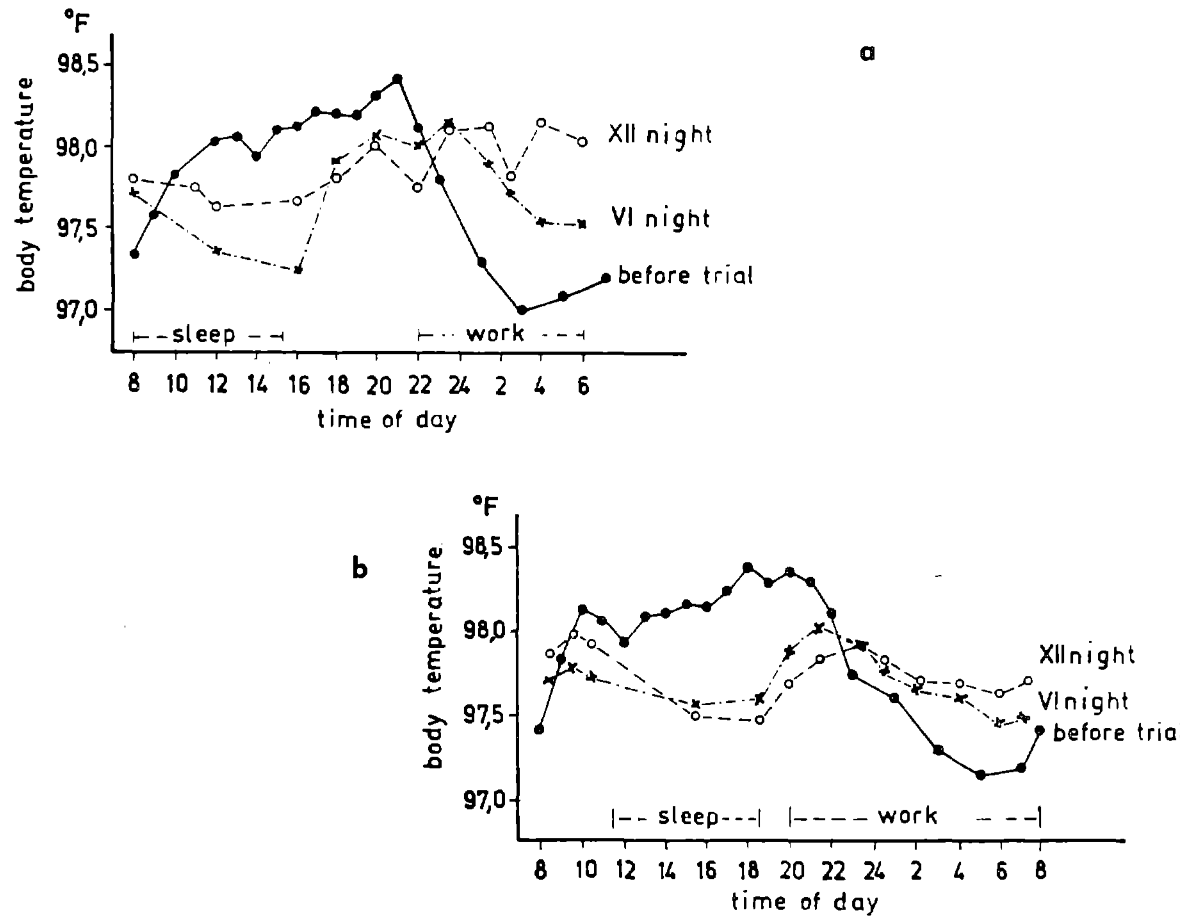


Figure 7. Alteration in temperature rhythm over 12 consecutive days on the night shift: (a) 8-hour night shift (Colquhoun, Blake, and Edwards, 1968b), (b) 12-hour night shift (Colquhoun, Blake, and Edwards, 1969).

Relatively small changes are observed in the rhythm of body temperature. This rhythm maintains its original course even after a long period on the night shift. It has been shown that there is some parallelism in circadian changes among body temperature, basal metabolism, general feeling of well-being, and performance on several mental and manual tests (46,138,139,172,199, 228). Therefore, very commonly, adaptation to night work is evaluated on the basis of changes in the circadian rhythm of body temperature. It does not seem, however, that this is the only reason for such a widespread application of these measurements. Measuring the body temperature is simple and the circadian rhythm of body temperature is well documented.

In many cases, the desynchronization among different circadian rhythms can be observed after altering the wake-sleep cycle. Desynchronizations result from changes in some rhythms, whereas others maintain their normal pattern (41,84,136, 158,159,186,271). A clear desynchronization of some rhythms was observed by Lewis and Lobban (159) in members of an expedition to Spitzbergen. Artificial "daily periods" of 21 or 27 hours duration were created by specially designed watches. The authors demonstrated that the rhythm of body temperature was adapted to the experimental daily routine more easily than those of urinary excretion of water and electrolytes. The rhythms of water, chloride, and potassium excretion were also desynchronized.

Froberg et al. (84), studying shift workers in a paper mill, observed some elevation of urinary adrenalin excretion after several days of night work, whereas the level of noradrenalin excretion remained unchanged (figs. 12a,b). Weitzman et al. (271), studied subjects living in an artificial lighting regimen for which night was created between 10 a.m. and 6 p.m. The diurnal rhythm of diuresis and urinary excretion of creatinine were inverted after a relatively short time, whereas the circadian rhythm of 17-OHCS excretion showed only a tendency toward an inversion in the second week of the experiment. However, body temperature sustained its normal pattern over the entire period of observation.

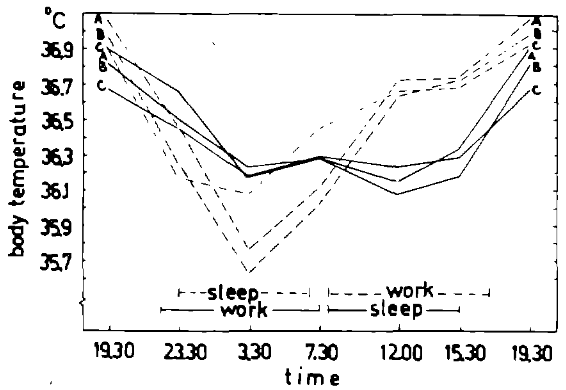


Figure 8. Average body temperature curves of three subjects (A, B, and C) during the day and night shifts. Night shift lasted 13 weeks and during this period, subjects (unaccustomed to night work) worked five nights per week (van Loon, 1963).

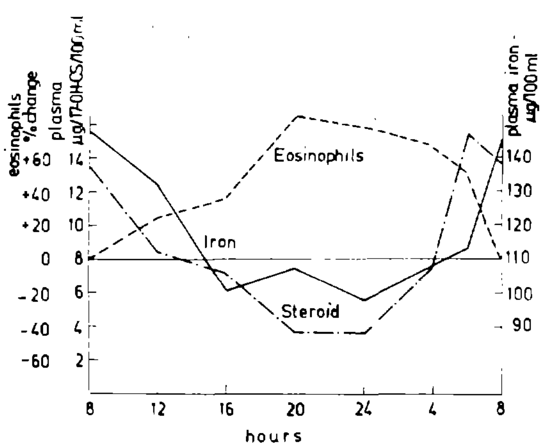
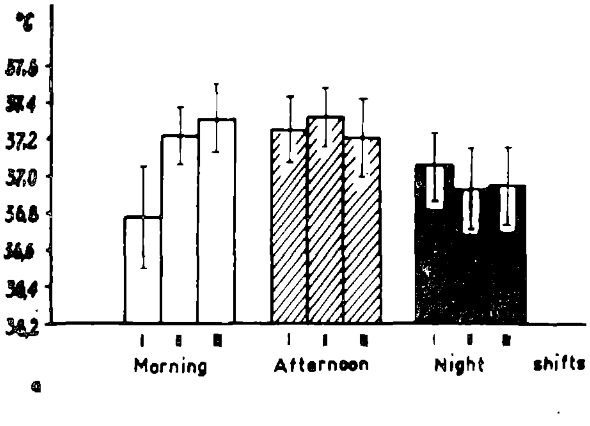
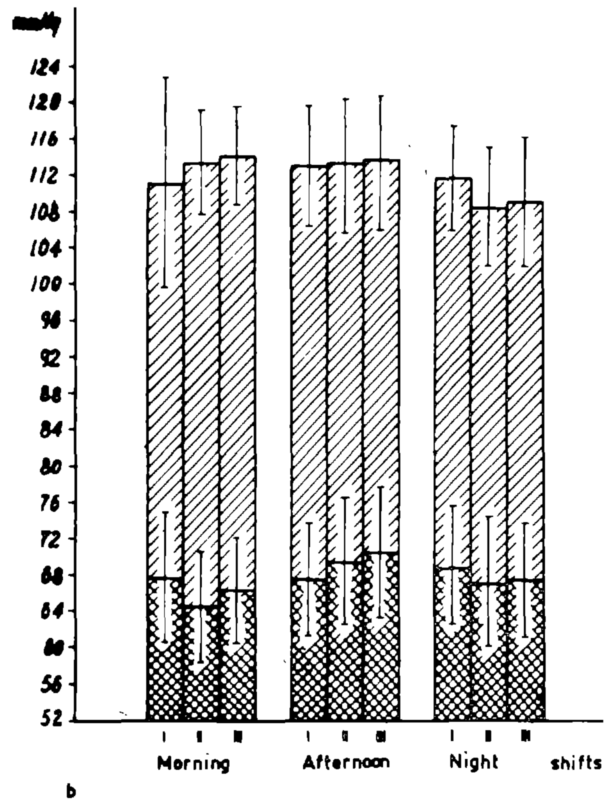


Figure 9. The mean variations of circulating eosinophils, iron level, and 17-OHCS in plasma for night workers, nurses, and watchmen, who had been working at night for at least 6 months prior to the experiment (Migeon et al., 1956).





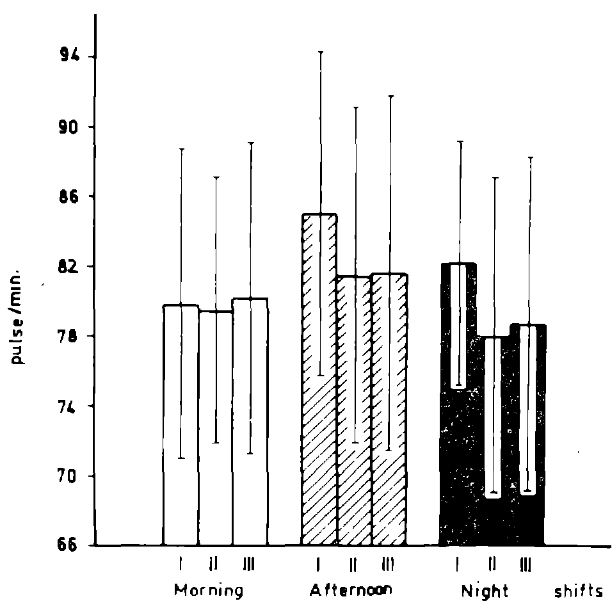


Figure 10. Curves of the average (a) body temperature, (b) systolic and diastolic blood pressure, and (c) heart rate of 50 shift workers (female spinners with at least 10 years of shift work experience). Measurements were performed at the beginning of the duty (I), after 4 hours (II), and after 8 hours (III) of work on the morning (5:30 a.m. to 1:30 p.m.), afternoon (1:30 p.m. to 9:30 p.m.), and night (9:30 p.m. to 5:30 a.m.) shifts (Wojtczak-Jaroszowa and Pawlowska, 1965).

In the period of desynchronization of rhythms, the susceptibility of the organism to various harmful factors increased. For a proper functioning of the body, not only is the transport of the "right material" to the "right places" and in the "right amounts" important, but it is equally vital that it happens at the "right time" (Halberg, 108).

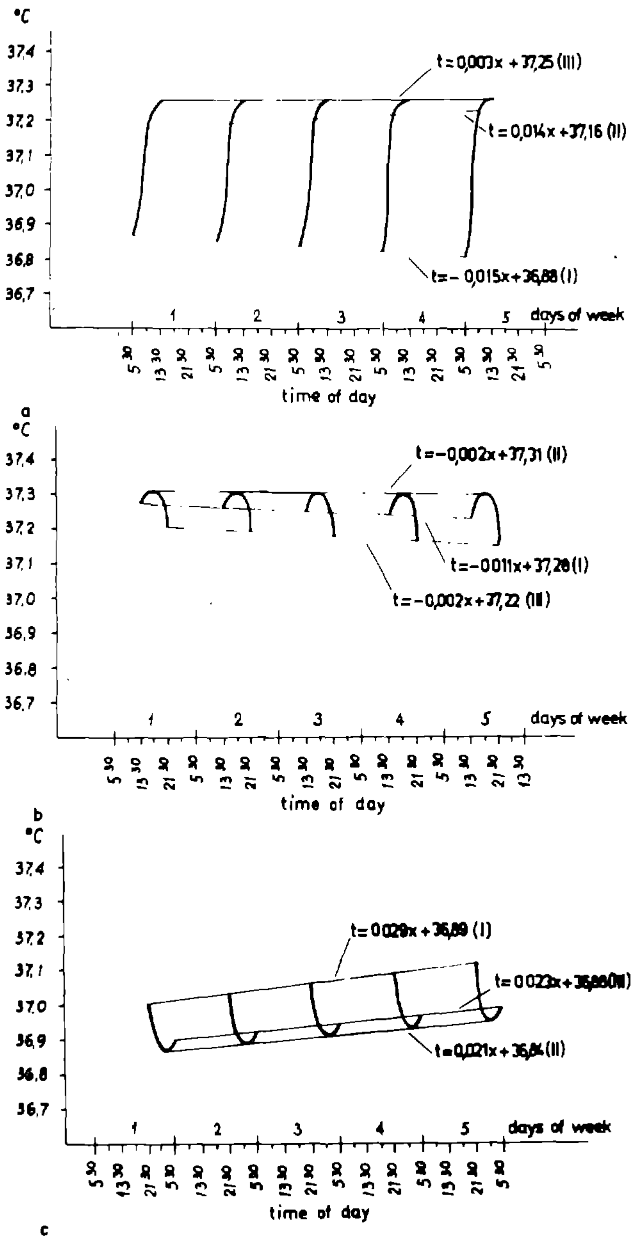
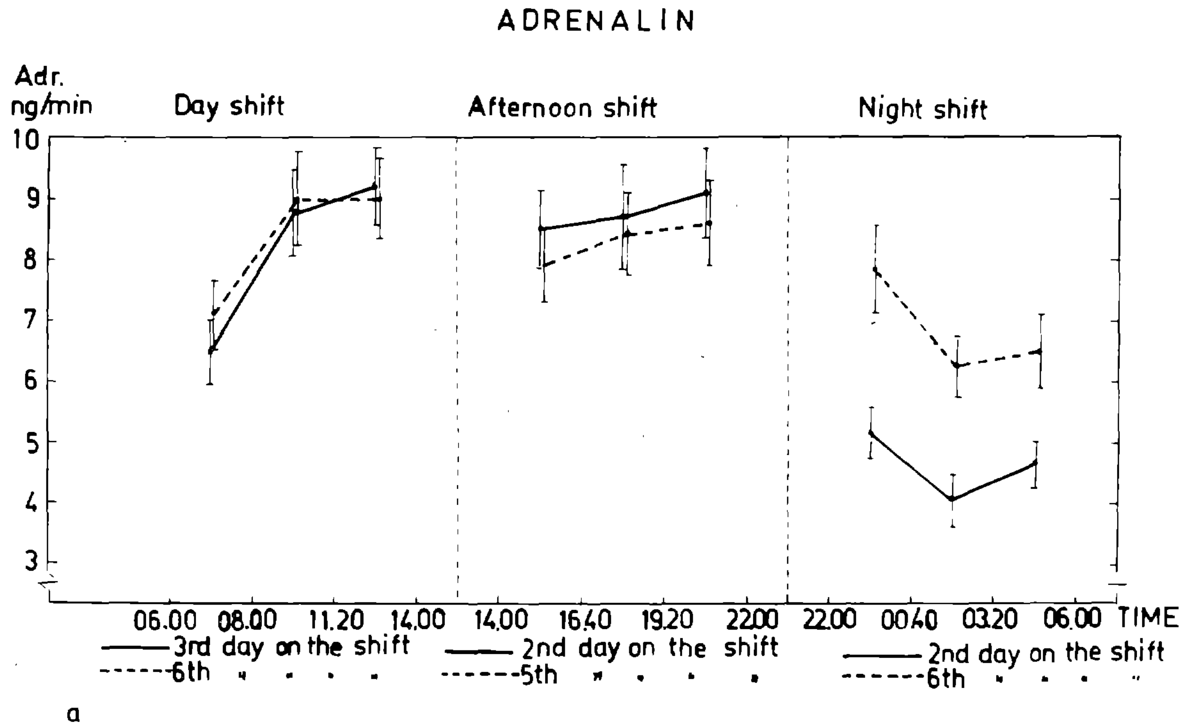


Figure 11. Body temperature curves of spinners (employed in a shift system with weekly rotation) during successive duties on (a) the morning, (b) afternoon, and (c) night shift. The regression lines have been drawn on the basis of the average values obtained (I) at the beginning, (II) after 4 hours, and (III) after 8 hours of work (Pawlowska-Skyba, Wojtczak-Jaroszowa, and Romejko, 1968).

Such desynchronization and abnormal diurnal variations of some functions have been observed during the course of several illnesses (6,39,146, 149). "It seems important to ask whether disturbances of the normal time relations among the circadian rhythms themselves are signals of the temporal limits to functional integration and adaptability and whether they might underlie disease. If so, recognition of variations in time relations among rhythms will contribute to the understanding of temporal maladaptations and diseases and thus to their eventual prevention or corrections" (Halberg, 108).

Thus, it is doubtful whether the symptoms of such desynchronization should be taken as an adaptation to night work. It rather requires raising the question of whether such an "adaptation" is at all desirable. It is also disputable that adaptation to night work may be evaluated on the basis of separate changes in some physiological rhythms. Even if some of them are inverted, the others (not studied) may maintain their previous pattern. On the other hand, it is impossible (especially in occupational conditions) to simultaneously measure the circadian rhythms of a large number of functions.

Eustace claimed that "men should not work for more than three days on any shift, as this means they will not have to invert rhythms to adapt to night shifts and then it will not be necessary to again revert to the normal diurnal rhythm" when returning to the day shift (74). In this situation, it seems more proper to talk about "tolerance" to night work rather than the "adaptation" to it. For an evaluation of night work tolerance, the social conditions of workers and their subjective feelings must be taken into consideration. However, feelings can not be accepted as an objective and quantitative measurement. For the objective assessment, it seems more appropriate to measure the work efficiency itself. According to Colquhoun's (46) research, programs in this field should give priority to the tests evaluating performance and the individual efficiency of workers. "There may be a very few situations where this work is itself of such a nature as to provide direct measures of 'true' efficiency, but in the majority of cases the latter will have to be assessed by interpolated tests. Thus, one of the major initial concerns of a laboratory research program should be the creation of tests which, though short, are nevertheless particulartly sensitive to circadian fluctuations, simple to administer, and also of high reliability" (46).



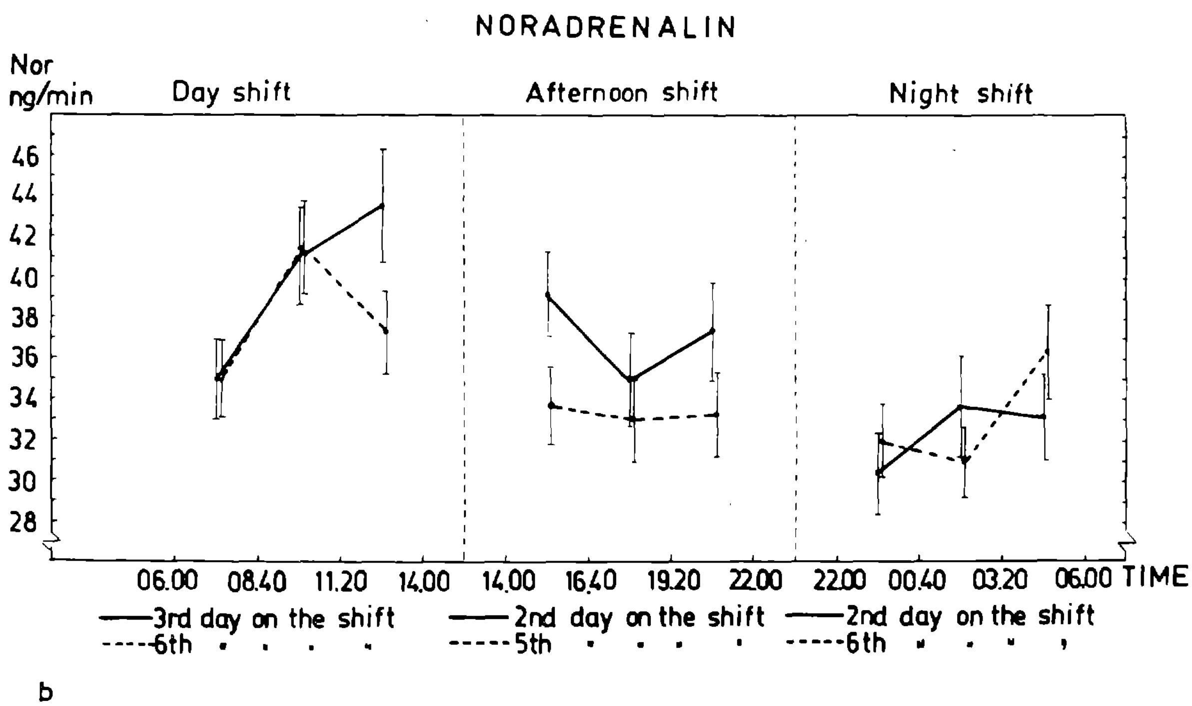


Figure 12. Urinary excretion of (a) adrenalin and (b) noradrenalin (means and standard deviations) for 42 subjects during day, afternoon, and night shifts. The samples of urine were collected at the beginning (i.e., on the second or third day) and at the end (i.e., on the fifth or sixth day) of the shift week (Froberg, Karlsson, and Levi, 1972).

CHAPTER II
PHYSICAL WORK

Despite the fact that heavy physical work is being gradually eliminated in industry and replaced by machines and automation, its role in many types of work such as coal mining, farming, and lumbering remains unquestioned. Also, muscular activity plays a basic role in numerous sports. The problem of circadian variations on the ability to perform physical work has been raised by many authors. The results of studies concerning the day-night variations in physical fitness and in physiological responses to external work will be presented in the last two sections of this Chapter. The mechanisms underlying these variations seem to be closely related to day-night variations in pulmonary and circulatory functions and in metabolic changes responsible for the energy supplying mechanisms. These are treated in the first three sections of this Chapter.

ROLE OF SOME FACTORS IN ENERGY TRANSFORMATION DURING PHYSICAL WORK IN THE DAY AND AT NIGHT

Large quantities of substrates are utilized by skeletal muscles during physical work. These substrates are derived mostly from the glycogen stores in the muscles and liver and from the triglycerides of adipose tissue. Prior to oxidation, the triglycerides are converted into free fatty acids (FFA) which pass into the blood. Mobilization of lipids exerts some protective role on the glycogen stores whose depletion may then be delayed during prolonged work. However, during heavy work, the glycogen stores are the major energy source. At the beginning of exercise, work capacity is related to the glycogen content of the working muscles. When the muscle glycogen level decreases, the glucose output from the liver then contributes the energy fuel for the muscles.

Among several factors that play an important role in metabolic changes during physical work, some show clear circadian periodicity, e.g., activity of the sympathetic nervous system, pituitary hormones, glycocorticoids, and catecholamines (192). Circadian variations have been shown for glycogen synthesis in the liver (86) and for the concentration of blood glucose (92). According to Gerritzen (93), the amplitude of day-night variations in the concentration of blood glucose was especially prominent in diabetics. The higher values were regularly noted in the morning and the lower ones in the evening regardless of the food intake which occurred every hour throughout the 24 hours.

The activation of both glycogenolysis and lipolysis during exercise is regulated by catecholamines. It has been shown that the catecholamine level in blood and urine increases during work. Catecholamines come to adipose tissue not only via circulating blood, but they are also released from the terminal nerve endings of the sympathetic nervous system, reaching the adipose depots in different parts of the body. In this way, the metabolism of fats is directly controlled by the sympathetic nervous system. Lipolysis is further sustained by adipokinetic pituitary hormones. However, the role of the growth hormone (HGH) is still unsure. It is suggested that the action of HGH depends upon increasing the sensitivity of adipose tissue to all adipokinetic agents. The increase in the plasma growth level of the hormone was observed under various physiological conditions with the physical work and sleep bringing about the greatest increase (57,209,227).

Because of the lower level of catecholamines and glycocorticoids, as well as, the diminished activity of the sympathetic nervous system at night due to circadian rhythm, the possibilities for mobilization of glycogen and lipids depots during physical work are probably diminished at night and muscle glycogen, then, is the main energy source. This can have a limiting effect on work capacity at night, especially in the case of strenuous exercise involving large muscle groups. Therefore, it seems likely that the tendency for severe hypoglycemia during heavy physical work could be higher at night than in the daytime. However, data which would confirm this presumption could not be found in the available literature. It also seems possible that, if in fact HGH would be released during physical work irrespective of the time of day, the mobilization of lipid sources could occur more easily at night than the utilization of glycogen. These hypotheses require experimental confirmation.

DAY-NIGHT VARIATIONS IN VENTILATORY CAPACITY

Pulmonary functions show clear circadian variations (37,182). Apart from the lower respiratory frequency, a reduction in the tidal volume, vital capacity, and alveolar ventilation is observed at night. In studies performed by Malinowski (1973) on female shift workers, the highest values of vital capacity were noted at the beginning of the afternoon shift at about 2 p.m. and the lowest values occurred at the end of the night shift, about 6 a.m. During the morning shift (6 a.m. to 2 p.m.), the vital capacity increased on the average by 22.6 ml, whereas it dropped by 83.0 ml and 211.1 ml during the afternoon (2 p.m to 10 p.m.) and night (10 p.m. to 6 a.m.) shifts, respectively.

In the studies of Burger et al. (37), respiratory function tests were performed on workers employed in a 2-shift system in which the duty lasted from 7:30 a.m. to 5 p.m. and from 10 p.m. to 7:30 a.m. The respiratory functions were measured twice per day, i.e., at the beginning and at the end of each shift. In these hours, no clear differences in respiratory function were observed on the tests performed at rest. However, significant differences were noted in respiratory minute volume when the measurements were carried out during cycling on the ergometer (at a work load of 110 watts). For the cycling, the values were significantly lower when the work was done at night.

Maximal breathing capacity also showed a downward trend at night. This was reflected by lower values of forced vital capacity and the forced expiratory volume (32,96,101,156). The graph depicting circadian changes of four ventilatory functions is presented in figure 13.

The diurnal changes in the forced expiratory volume (FEV) are manifested even in workers with long experience in the shift system. The amplitude of circadian variations of FEV in healthy subjects amounts to about 0.1 L (55). It is noteworthy (260) that in people who work in the dusty environment of cotton mills, as well as in subjects with byssinosis, and apart from usually higher values of $FEV_{0.75}$ in the daytime, the reduction of the $FEV_{0.75}$ during the work period on every shift was observed (fig. 14).

DAY-NIGHT VARIATIONS IN CIRCULATORY FUNCTIONS

Several functions of the circulatory system remain at a lower level at night (37,58,87,117,132, 135,262) even in workers with long shift work experience. This refers particularly to arterial systolic pressure and pulse pressure. Less regular changes are seen in the heart rate. The circadian variations in arterial systolic pressure parallel the variations in arterial blood flow which have also been demonstrated (128).

Diminution of pulse pressure during the night results from a greater reduction of the systolic than of the diastolic blood pressure (23,182,201, 283,284). In our studies performed on shift workers (spinners), the lowest values of pulse pressure were during the night shift, after midnight (fig. 15). This was accompanied by a feeling of tiredness and sleepiness. The diurnal variations in blood pressure were more pronounced in individuals with hypertension (figs. 16a,b). This might be the cause of the poorer tolerance to night work by the hypertensive subjects (217,231).

In spite of parallel circadian changes in heart and respiratory rates, the quotient; pulse rate/respiratory rate ($Q_{P/A}$), also shows circadian changes as a result of a relatively greater decline of heart rate than in respiratory rate at night (114). During night sleep this quotient oscillates around the value of 4. Early in the morning, even in people refraining entirely from any physical activity, $Q_{P/A}$ increases and in the daytime it remains at a higher level than at night (fig. 17). The circadian periodicity of $Q_{P/A}$ could be abolished by administration of Somnifen.

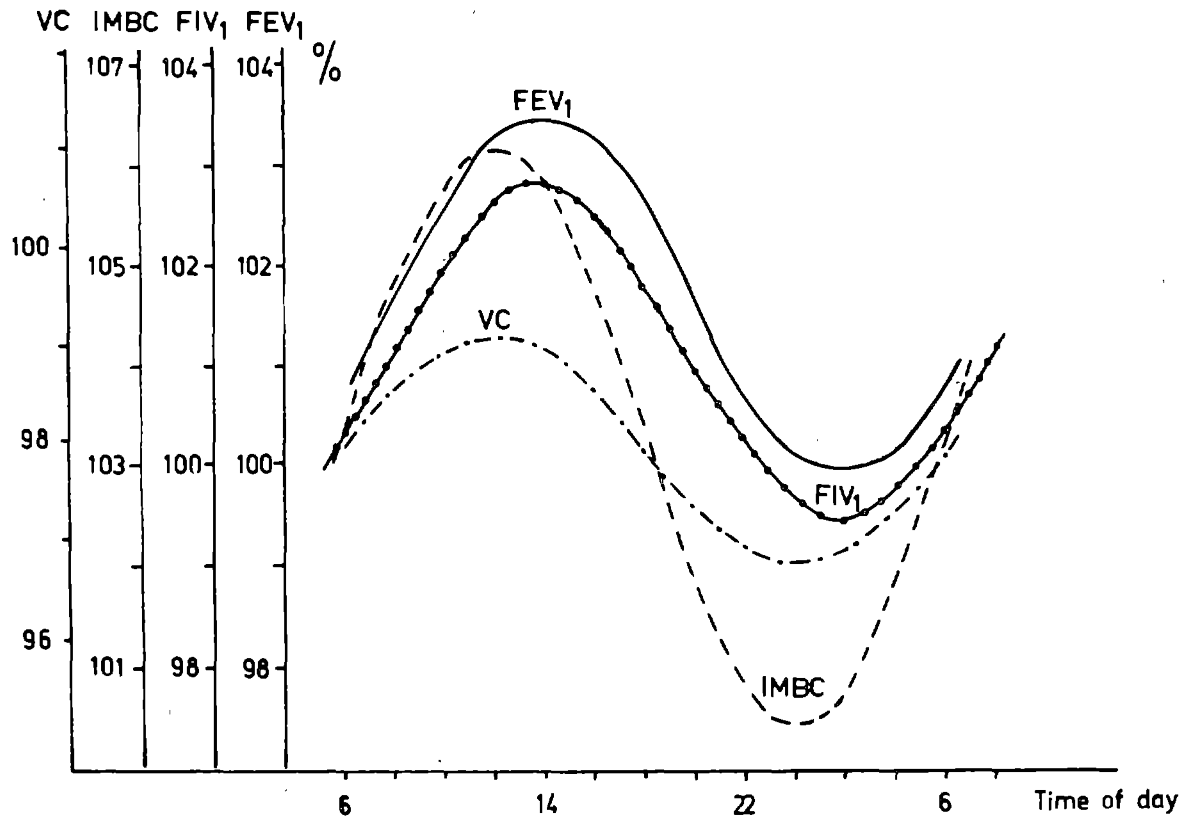


Figure 13. Average curves of indirect maximal breathing capacity (IMBC), vital capacity (VC), forced expiratory volume, 1 second (FEV_1), and forced inspiratory volume, 1 second (FIV_1). The investigations were performed on 16 healthy males (20 to 25 years old) unaccustomed to night work, who were examined every 2 hours (Gielec, 1973).

FITNESS AND ORTHOSTATIC TESTS IN THE DAY AND AT NIGHT

There is some disagreement in the results of fitness and orthostatic tests when day and night experiments are compared (21,133,135,151,182, 251,257,258,279). Even the same authors, when using different tests of fitness sometimes obtain contradictory results. Thus for example, Klein, Wegmann, and Bruner (135) observed that tilt table tolerance was relatively better in the afternoon (between 3 p.m. and 7 p.m.) than early in the morning (between 3 a.m. and 6 a.m., fig. 18a). In the same people, the Schneider's index and the V_{O2} max predicted using the Astrand and Rhyming nomogram were relatively higher at night than in the afternoon (fig. 18b).

In the Crampton's test, higher values were usually obtained at night (21,22), whereas the results on Lehmann and Michaelis test (Amplituden-Frequenze Product) indicated lower physical fitness at night (151,153,279).

In general, for fitness tests in which short or frequently altered work loads are applied, as in the Miller's test (Leistungs-puls Index, LPI) or in some modifications of the PWC_{170} test (Physical Work Capacity), results suggest that physical fitness is higher at night (258,280). The circadian changes in PWC_{170} are presented in figure 19a. Also in our own studies (in press), in which the PWC_{170} test has been applied in the form modified by Macnab, Conger, and Taylor (166) with the work load changed every 4 minutes, higher values were obtained at night than in the daytime (Table 1).

In the PWC_{170} test, the index is calculated as the work load that produces a pulse rate of 170 beats/min. Consequently, the higher index values obtained at night could result from a lower heart rate at a given external work load as compared to the daytime. This finding seems to derive from

TABLE 1

Subject	$\frac{x_2 - x_1}{x_1} \times 100$	Subject	$\frac{x_2 - x_1}{x_1} \times 100$	Subject	$\frac{x_2 - x_1}{x_1} \times 100$
1.	+ 8.8	20.	− 1.7	39.	+ 36.7
2.	− 1.1	21.	+ 8.6	40.	− 1.9
3.	+ 13.8	22.	+ 17.8	41.	+ 6.0
4.	+ 27.6	23.	− 5.4	42.	+ 3.5
5.	+ 32.1	24.	− 12.6	43.	− 10.1
6.	− 5.7	25.	− 1.3	44.	+ 8.8
7.	+ 13.9	26.	+ 14.3	45.	+ 7.1
8.	+ 67.8	27.	− 1.8	46.	+ 10.3
9.	+ 12.7	28.	+ 4.5	47.	+ 3.7
10.	+ 1.0	29.	+ 18.3	48.	− 1.0
11.	− 19.1	30.	− 2.1	49.	+ 5.3
12.	+ 8.7	31.	− 6.6	50.	+ 0.2
13.	+ 25.5	32.	+ 15.3	51.	+ 5.5
14.	+ 21.9	33.	+ 6.2	52.	+ 22.3
15.	+ 1.5	34.	+ 21.9	53.	− 1.0
16.	+ 19.6	35.	+ 14.9	54.	+ 19.8
17.	+ 2.9	36.	− 3.7	55.	+ 9.2
18.	+ 14.4	37.	+ 3.8	56.	+ 6.0
19.	+ 15.8	38.	+ 15.3		

Table 1. The differences in PWC_{170} test between day (x_1) and night (x_2) experiments. The experiments were performed between 9 a.m. and 1 p.m., and 1 p.m. and 5 a.m. in the day and at night, respectively. The values were calculated individually, taking the day values as 100 percent (280).

two circumstances: the short duration of every work load used and the lower resting heart rate during the night than in the daytime. In this situation, the work lasting only 4 minutes could be sufficient to reach the steady-state level in the daytime, but might be too short to do so at night. This presumption is confirmed by our studies (unpublished), in which a given external load on the ergometer was applied to the same people both in the day and at night. In these experiments we have observed that to reach a steady state level, the work had to be prolonged beyond the 6-minute period more often during the night sessions than in the day. It has been assumed that the steady state level was reached if the difference in heart rate in two successive minutes did not exceed 5 beats per minute.

A similar explanation also seems plausible to elucidate the day-night variations in the LPI. This index relies heavily on the changes in pulse rate during the test. Voight et al. (258), demonstrated higher values of the index during the day relative to the values obtained at night, which suggested better physical fitness at night (fig. 19b). Considering these findings, the authors discussed whether in fact physical working capacity is higher at night, or whether there is only a slower adaptation of the circulatory system to the requirements of physical work.

In fact, it seems that because of day-night variations in the circulatory system, its adaptation to a given work load can proceed more quickly during the day than at night. It is important also that the parameters of circulatory and respiratory functions are at a lower resting level at night than during the day. Usually, only the absolute values of the physiological parameters are considered. Thus, it seems to be more appropriate to compare the net increases (differences between working and resting level) of physiological parameters rather than the absolute values when day-night variations are evaluated. The requirements that the readings represent a steady state level, both in the day and at night, is also indispensable for comparable results.

Klein, Wegmann, and Bruner (135) in discussing possible reasons for the observed discrepancies when indirect fitness tests are used for the assessment of circadian variation in physical work capacity, remarked: "All indirect fitness tests are based on the fact that subjects with a higher performance capability for physical exercise, e.g., trained people, have lower heart rate levels both at rest and during exercise. Consequently, in such tests, lower heart rates are scored better if measured under the same experimental conditions. If we keep these facts in mind and consider the periodicity in heart rate . . . the described

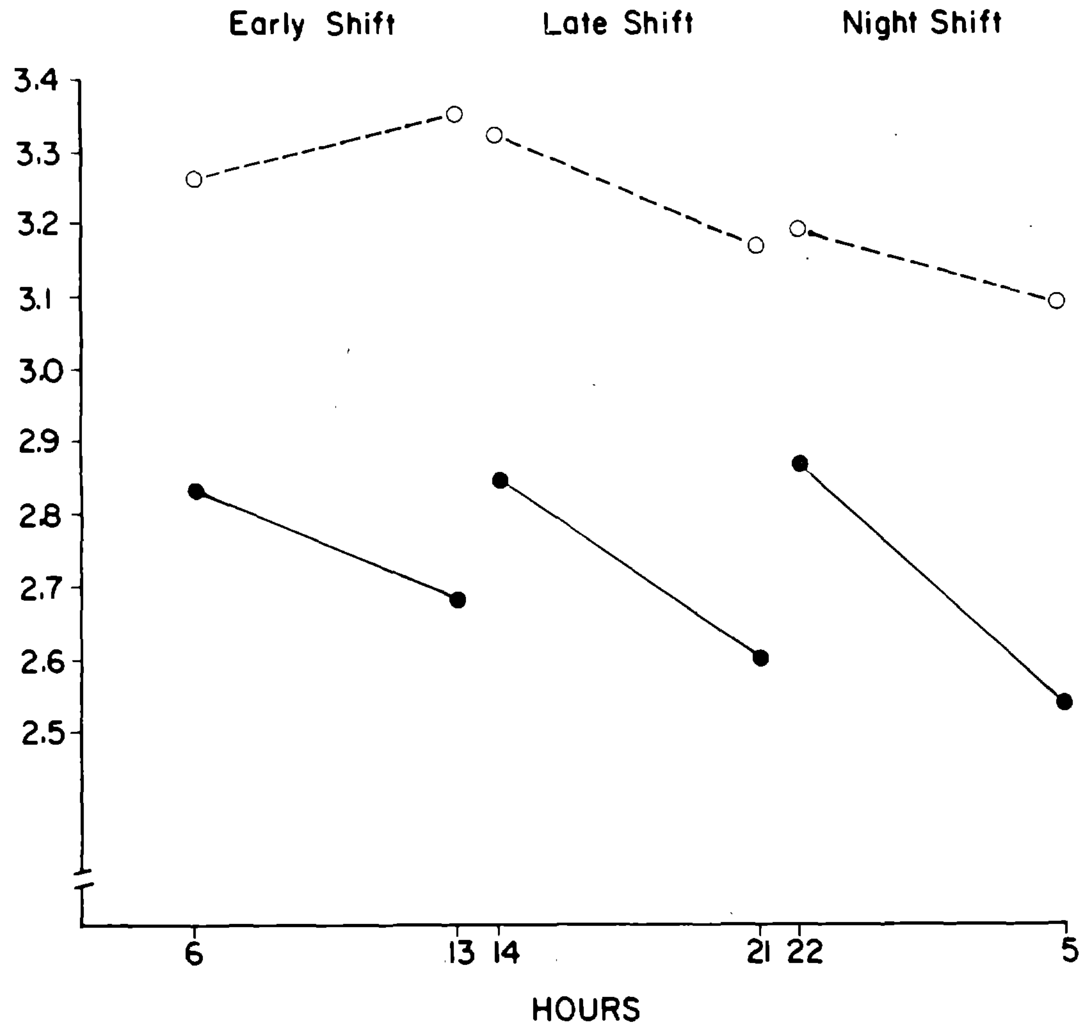


Figure 14. Mean changes in $FEV_{0.75}$ during shift work for (a) workers in non-dusty factories and (b) workers with byssinosis employed in card and blow rooms (Walford et al., 1966).

circadian course for the indices of fitness can be demonstrated, but only as a result of these interrelations." Their conclusion that: "The discussion of this phenomenon should begin with the statement that indices of fitness were measured and not fitness itself " seems fully appropriate.

Caution should be exercised in drawing any firm conclusions with regard to diurnal variation of physical work capacity estimated on the basis of V_{O2} max, as predicted using the Astrand and Ryhming nomogram (15). The V_{O2} max values calculated in this way by Klein, Wegmann, and Bruner (135), were somewhat higher at night. In our experiments performed on 90 men, no statistical differences were observed (Wojtczak-Jaroszowa, Banaszkiewicz, and Makowiec-Dabrowska, 279). The Astrand and Ryhming nomogram, is based on the observed relationship between heart rate and oxygen uptake during increasing levels of submaximal work, and the oxygen uptake during maximal work. However, the data which had been used for these calculations were based on the results of daytime experiments. These interrelationships could expectedly be different during the night hours due to circadian variations in circulatory, metabolic, and pulmonary functions.

When using this nomogram for assessing circadian variations in a physical work capacity, it must be assumed, a priori, that these daytime relationships also hold for night work. However, recent studies by Wahlberg and Astrand (259) seem to indicate that these relationships can vary at night by demonstrating that the reduced maximal heart rate at night was not accompanied by corresponding change in the oxygen uptake. In this study, the oxygen uptake was determined at high work rates which were predicted from the nomogram as the maximal load, at which no differences were seen in oxygen uptake between

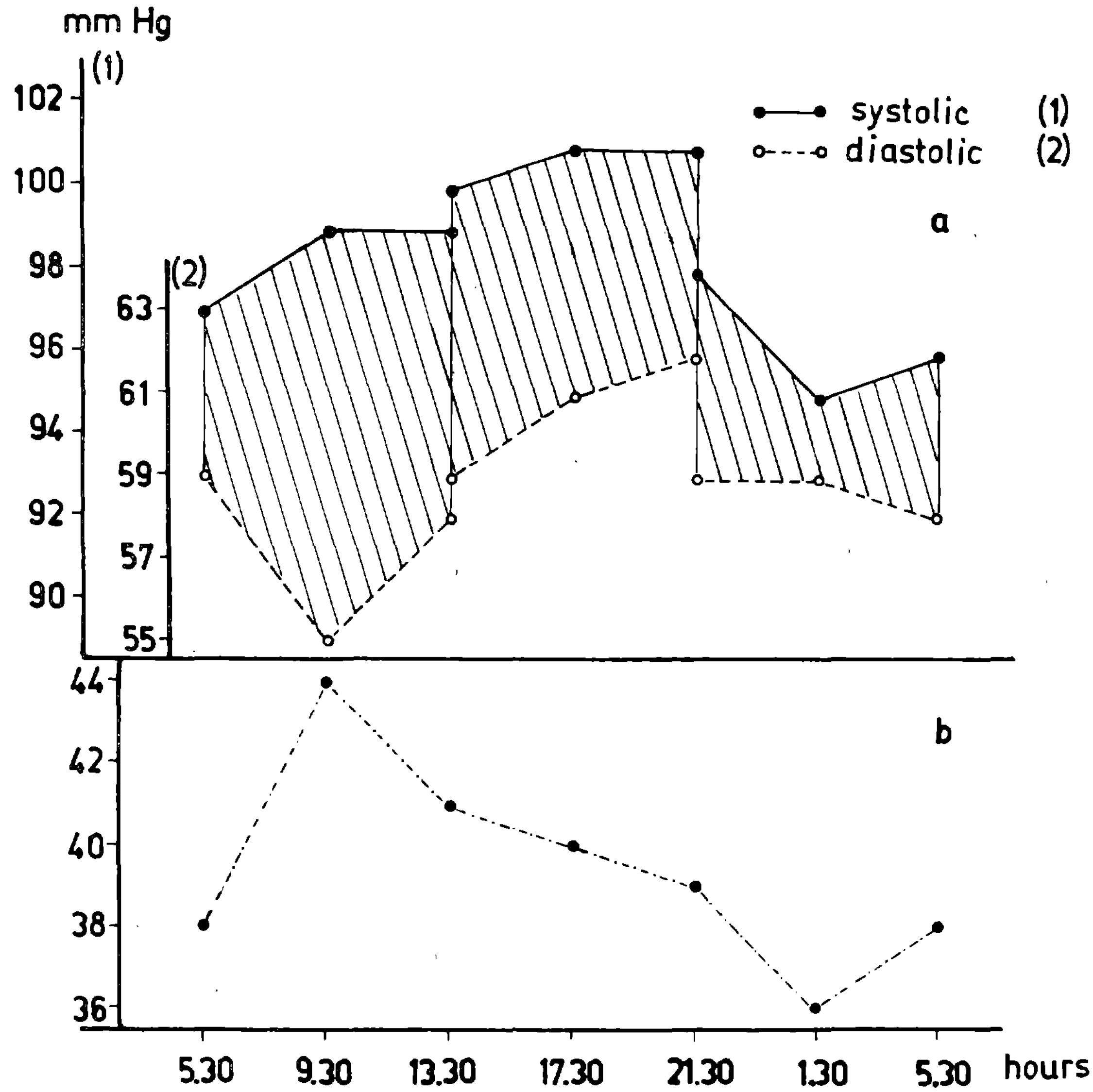


Figure 15. Average curves of blood pressure (a) and pulse pressure (b) of 50 female spinners. The measurements were performed during the morning (5:30 a.m. to 1:30 p.m.), afternoon (1:30 p.m. to 9:30 p.m.), and night (9:30 p.m. to 5:30 a.m.) shifts (Wojtczak-Jaroszowa and Pawlowska, 1965).

night and day sessions. These observations would suggest that there were no day-night variations in $\dot{V}_{O_2}$ max.

In our own studies (Wojtczak-Jaroszowa and Banaszkiewicz, in press), the commonly accepted method was used for determining $\dot{V}_{O_2}$ max; the work load was gradually increased up to a supramaximal load to insure that oxygen uptake really reached the maximal value. This procedure was used in both the day and the night experiments. The study was performed on 26 healthy males (athletes), aged 16 to 28 years, while cycling on the ergometer. In those individuals $\dot{V}_{O_2}$ max was also predicted for day and night using the Astrand and Ryhming (15) nomogram and the PWC $_{170}$ test was performed. The experiments were performed between 9 a.m. and 1 p.m., and again between 1 a.m. and 5 a.m. Prior to the testing sessions all the men were familiarized with the experimental procedures and before the maximal load was applied, they performed the submaximal exercises several times on the ergometer. To avoid undue tired periods prior to the night experiments as compared with day ses-

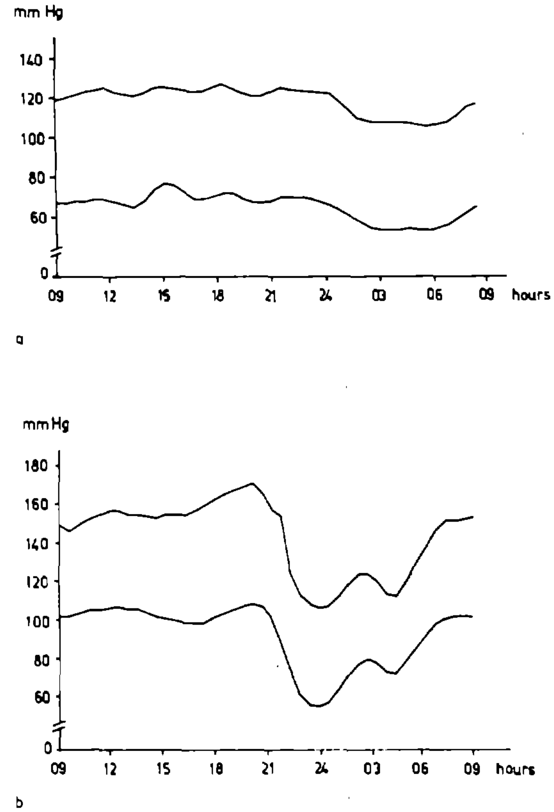


Figure 16. Twenty-four hour records of the blood pressure of (a) normotensive, pregnant women (32 weeks gestation) and (b) chronic hypertensive, pregnant women (31 weeks gestation). Readings were taken every 5 minutes (Seligman, 1971).

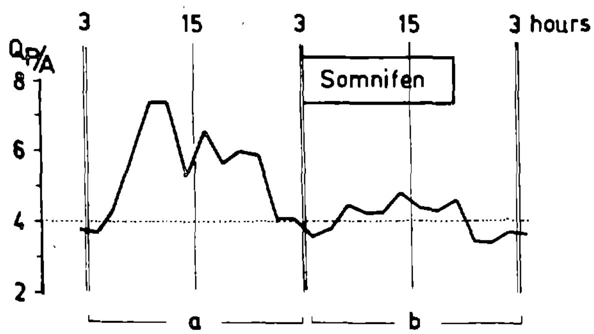
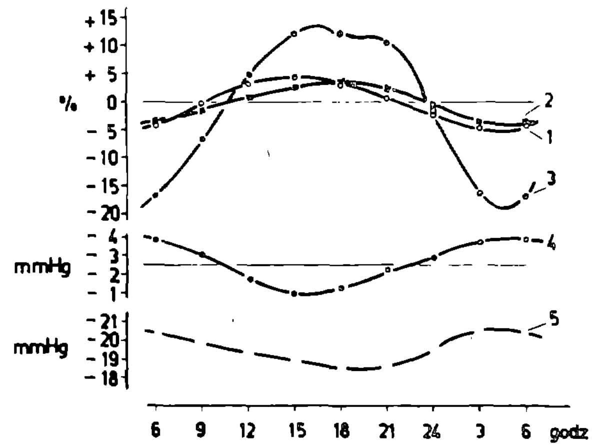


Figure 17. Circadian changes in the quotient $Q_{P/A}$ (pulse rate/respiratory rate) in a resting man: (a) before and (b) after administration of Somnifen (Hildebrandt, 1955).

sions, the subjects rested for a few hours during the afternoons preceding the night sessions (according to interviews, everyone slept for at least 2 to 3 hours before each night session). A light meal was consumed not later than 2 hours before the beginning of both the day and night sessions. Each test was performed on separate days or nights.



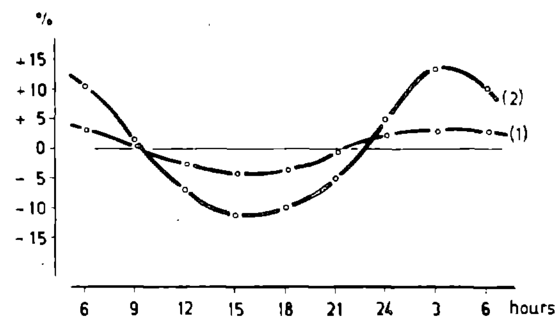
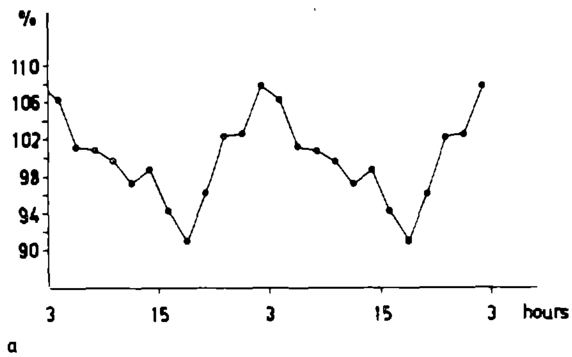


Figure 18a. Circadian rhythm of cardiovascular responses to tilting: (1) heart rate, (2) systolic blood pressure, (3) pulse pressure, (4) change of systolic blood pressure, and (5) change of pulse pressure. The values of each of the parameters were averaged "vertically" to a mean 24-hour cycle for the total group (Klein, Wegmann, and Bruner, 1968).
Figure 18b. Circadian rhythm of (1) $\dot{V}_{O_2}$ max predicted by Astrand and Rhyming's nomogram and (2) Schneider's index (Klein, Wegmann, and Bruner, 1968).

As it is shown in Table 2, $\dot{V}_{O_2}$ max determined directly was higher in the daytime than at night. Of the 24 subjects, 2 had a higher $\dot{V}_{O_2}$ max at night, 2 showed no day-night difference and in 20 the night values were 4 to 14.6% lower than the day values. Moreover, in two subjects not included in the table, the highest attainable load on the ergometer was too low (60 revolutions per minute) to reach maximal oxygen uptake in the daytime tests, whereas it was sufficient during the night experiments. For the included 24 people, the average of $\dot{V}_{O_2}$ max was 3.8 L/min and 3.6 L/min for the day and night experiments, respectively. These small differences were statistically significant at $p < 0.001$. Taking the day values as 100 percent the calculated $\dot{V}_{O_2}$ max was about 5 percent lower during the night experiments. At



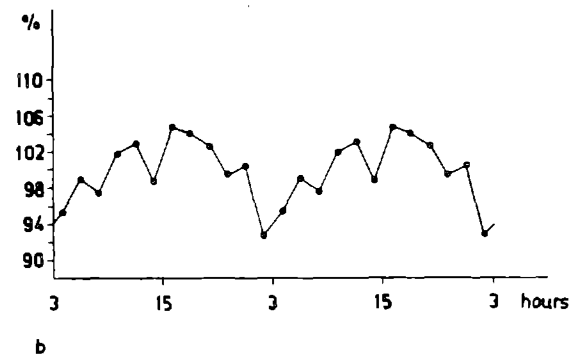


Figure 19. Circadian rhythm of (a) PWC_{170} and (b) LPI. The values of indices were calculated individually as a percentage of a mean 24-hour period for 20 young subjects (Voight, Engel, and Klein, 1968).

the same time, no significant difference was observed in maximal heart rate between day and night experiments.

The results of the other two tests performed with the same men were not uniform. The values of PWC_{170} were significantly lower ($p = 0.003$) in the daytime (a average 1249 kgm/min). The values of predicted $\dot{V}_{O_2}$ max showed no significant difference with an average 3.7 L/min and 3.8 L/min for day and night experiments, respectively. Thus, we concluded that the physical fitness was higher in the daytime as compared to the night, however, these differences were not apparent when indirect fitness tests were used. These results confirm the view that indirect fitness tests may not reveal true day-night variations in physical work capacity and that the results of such tests can be misleading.

DAY-NIGHT VARIATIONS IN PHYSIOLOGICAL RESPONSES TO PROLONGED PHYSICAL EFFORT

For practicality, it is important to know whether there are day-night differences in physiological responses to prolonged physical work. Astrand and Rodahl (16) demonstrated that the load which exceeded about 50 percent of the subject's maximal oxygen uptake could be too high if the physical activity was continued for many hours. Generally, a 30 percent load is accepted as a limiting value for prolonged physical effort in occupational conditions (147). Because of day-night variations in physical fitness, the question arises of whether the same limits should be accepted for both day and night work. In other words, does a given level of external work lasting for several hours cause the same physiological

TABLE 2

Subject	$\frac{x_2 - x_1}{x_1} \times 100$	Subject	$\frac{x_2 - x_1}{x_1} \times 100$	Subject	$\frac{x_2 - x_1}{x_1} \times 100$
1.	0.0	9.	− 2.6	17.	− 9.3
2.	− 5.3	10.	− 6.3	18.	− 5.1
3.	− 5.4	11.	− 7.3	19.	− 5.1
4.	− 2.7	12.	0.0	20.	− 2.3
5.	− 14.6	13.	+ 5.1	21.	− 3.0
6.	− 11.9	14.	− 4.9	22.	− 3.0
7.	− 2.9	15.	− 12.2	23.	+ 3.0
8.	− 9.8	16.	− 5.3	24.	− 5.9

Table 2. The differences in $\dot{V}_{O_2}$ max determined by maximal exercise test between the day (x_1) and night (x_2) experiments. The experiments were performed between 9 a.m. and 1 p.m., and 1 p.m. and 5 a.m. in the day and at night, respectively, taking the day values as 100 percent (280).

strain during the day as when performed at night. No available literature could be found to answer this question.

The studies performed in the author's laboratory (167,277,279) showed that physiological strain of a given external work load is higher at night than during the day. The studies were carried out in two series. In the first one, the physiological parameters were recorded in 30 healthy males (19 to 22 years of age) cycling for 30 minutes on the ergometer. The physical load was adjusted to be 50 percent of the individual $\dot{V}_{O_2}$ max which, as estimated directly according to Astrand and Ryhming nomogram, amounted to an average of 3.7 L/min. All subjects were examined three times during the day (between 9 a.m. and 1 p.m.) and three times at night (between 1 a.m. and 5 a.m.) on separate sessions. The sleep pattern and meal regimen were similar to those described previously in regard to the estimation of $\dot{V}_{O_2}$ max.

It was demonstrated that after the fifth minute of riding, both the oxygen uptake and carbon dioxide production were maintained at a slightly higher level during night than during the day sessions. The average difference in oxygen uptake was about 30 ml/min at the beginning of the work (between the fourth and eighth minute of cycling) and reached 75 ml/min at the end of riding (between the 26th and 30th minute). However, there were no statistically significant differences between day and night levels of the physiological functions. Nevertheless, statistically significant variations were detected when net values (work minus rest values) were calculated (figs. 20a,b,c). Namely, net oxygen uptake and net energy expenditure amounted on the average to 45327 ml and 234 kcal, and 43132 ml and 222 kcal for 30 minutes cycling at night and during the day, respectively ($p = 0.005$ for oxygen uptake, and $p = 0.022$ for energy expenditure). The cardiac work cost was also calculated as a sum of heart beats during the working period above resting level. It was shown that the difference in cardiac work cost between day and night sessions was not large but it was statistically significant ($p = 0.019$). On the average, the heart rate values were higher by 73 beats for night experiments than for day sessions. Taking the day value of each parameter as 100 percent, the night values were higher by about 5 percent.

In order to estimate the physiological "cost" of night and day work, mechanical efficiency of work was determined according to the formula:

$$\eta = \frac{We \times 100}{M - RM}$$

η = mechanical efficiency
We = external work performed
M = total energy expenditure
RM = resting energy expenditure

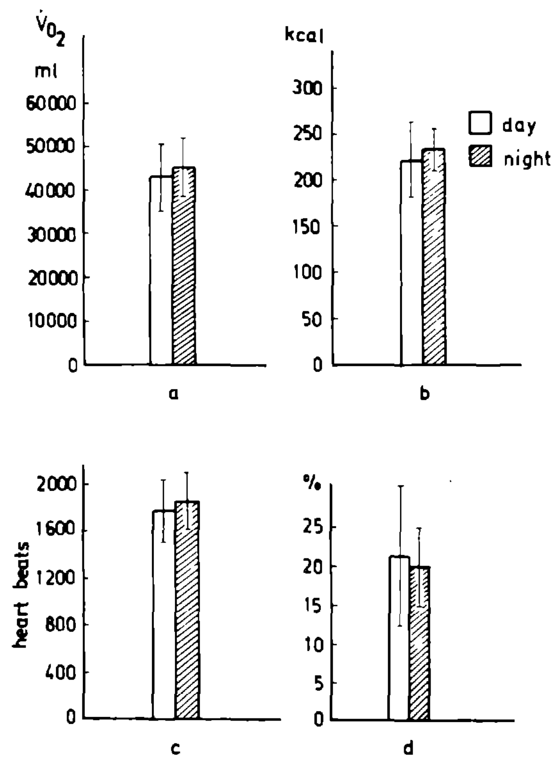


Figure 20. The changes in (a) net oxygen uptake and (b) net energy expenditure (total values above resting level for 30 minutes of riding); (c) cardiac work cost (the sum of heart beats occurring during the working period above resting level); and (d) mechanical efficiency of work. The work was performed during the day between 9 a.m. and 1 p.m., and at night between 1 a.m. and 5 a.m. Average values for 30 young, healthy males (Wojtczak-Jaroszowa, 1973a).

Because of the higher energy expenditure during night experiments (at constant external work in day and night sessions), mechanical efficiency was significantly lower at night ($p = 0.004$, fig. 20d). Thus, the given external work was performed less "economically" at night than during the daytime, and the physiological "cost" was higher at night.

The second series in the study comprised 17 shift workers who had been employed in a glass factory for many years. Because each worker repeated the same kind of operation on every shift, and, each factory was making the same sort of glass all the time, the individual load seemed to be similar on every shift. The workers were examined at rest prior to the morning, afternoon, and night shifts (5:30 a.m., 1:30 p.m., and 10:30 p.m., respectively) and during normal work between the second and fourth, and between the sixth and eighth hour of work on each shift (i.e., about 9 a.m. and 1 p.m. on the morning shift, about 5 p.m. and 9 p.m. on the afternoon shift, and about 1 a.m. and 5 a.m. on the night shift). The work required about 25 to 30 percent of the individual's $\dot{V}_{O_2}$ max as predicted from the Astrand and Ryhming nomogram, an average of 2.4 L/min.

The lowest and the highest oxygen uptake at rest was observed before the morning and afternoon shift (5 a.m. and 1 p.m., respectively). This is in accord with data from literature, which demonstrate that the resting metabolic rate is lower at night than in the daytime (14,148). At work, however, pulmonary ventilation, oxygen uptake, and energy expenditure (calculated from O_2 consumption) were significantly higher during the night shift as compared with daytime, morning, and afternoon shifts (Table 3, fig. 21). These differences were statistically significant in terms of oxygen uptake ($p = 0.015$ and $p = 0.002$ when morning and night, and afternoon and night measurements were compared, respectively) and of energy expenditure ($p = 0.008$ and $p = 0.002$, respectively). If the day shift values are taken as 100 percent, the difference in oxygen uptake between day and night measurements was about 10 percent. It is noteworthy, that even though the speed of work on the night shift was slightly lower, the energy expenditure calculated per unit of work was higher ($p = 0.002$) than during the day.

Thus, the results obtained under these experimental and occupational conditions demonstrate day-night differences in physiological responses to a given external work load. These results were recently confirmed by our further studies performed under standardized conditions in which a constant dietary regimen was maintained. The results seem to be important in a practical sense, especially with regard to prolonged work performed by people with low physical work capacity. In our observations, for well trained men doing heavy work for 30 minutes, the day-night differences in physiological responses amounted to about 5 percent of daytime values (net values) rising to about 10 percent for subjects with lower work capacity performing uninterrupted work for many hours. Perhaps, the differences in energy cost of physical work performed during the day and at night would be still greater for heavier work and for people with lower physical work capacity. As a result, the physical load corresponding to moderate work during the day may overlap with a heavy one when it is performed at night. Consequently, an external load equaling 30 percent of $\dot{V}_{O_2}$ max in the daytime may significantly exceed this limit when performed on the night shift; in addition the $\dot{V}_{O_2}$ max is lower at night than during the day.

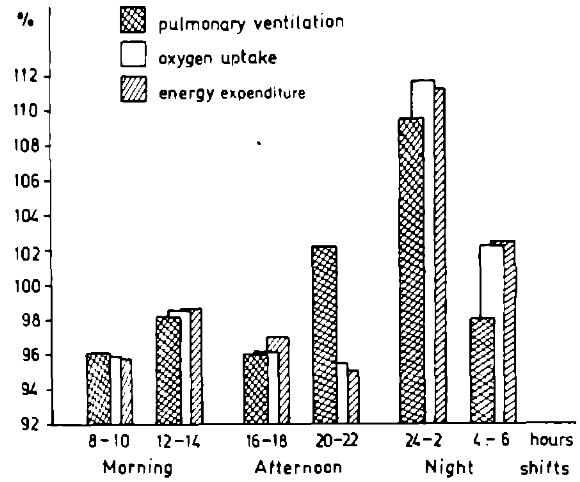


Figure 21. Pulmonary ventilation, oxygen uptake, and energy expenditure during occupational work on three shifts (See Table 3; Makowiec-Dabrowska, Wojtczak-Jaroszowa, and Brykalski, 1967).

TABLE 3

Shift	Hours	Ventilation		Oxygen uptake		Energy expenditure	
		l/min	%	ml/min	%	kcal/min	%
Morning	8:00-10:00	19.62±1.68	96.1±2.4	599±52	95.9±2.6	2.94±0.52	95.8±2.3
	12:00-14:00	19.89±1.54	98.2±2.0	609±46	98.6±2.7	3.00±0.22	98.7±2.4
Afternoon	16:00-18:00	19.86±1.93	96.0±2.0	598±51	96.1±2.1	2.97±0.24	97.0±2.2
	20:00-22:00	21.27±2.21	102.2±3.3	597±53	95.4±2.0	2.93±0.24	95.0±2.4
Night	0:00-2:00	22.73±2.47	109.5±5.2	694±68	111.7±5.1	3.41±0.34	111.2±5.1
	4:00-6:00	20.03±1.83	98.0±2.0	621±41	102.3±3.5	3.07±0.20	102.4±3.3

Table 3. Mean values (and standard errors) of pulmonary ventilation, oxygen uptake, and energy expenditure (17 shift workers). The measurements were performed during the work on morning shift (about 9 a.m. and 1 p.m.), afternoon shift (about 5 p.m. and 9 p.m.), and night shift (about 1 a.m. and 5 a.m.). Percentages were calculated individually, taking the day values as 100 percent (167).

CHAPTER III

MENTAL, SENSORY-MOTOR, AND MANUAL PERFORMANCE

"Man, who until recently to satisfy his elementary needs had to perform work requiring considerable muscular effort, in the last years forms a special species — homo sedentarius"
— S. Kozlowski

Technological progress in contemporary industry has changed the character of work in many respects. With increasing frequency, industrial work requires mental, sensory-motor, and precision manual performance instead of physical effort. The efficiency, or even the safety of work, may depend upon the correct reading of signals and fast and appropriate responses to stimuli other than the application of physical strength and endurance. Many jobs created by the introduction of automated systems involve prolonged and continuous inspection activities, and demand constant vigilance and mental alertness. Work of this kind has recently evoked particular interest among physiologists and psychologists. Inspection tasks have been classified by Kano (129) into the following four categories:

"1. Tasks mainly characterized as repetitive and continuous inspection in mass production.
2. Tasks required to monitor signals or targets presented on displays, such as radar operations.
3. Tasks required to assess the qualities of materials or products in order to sort them into categories.
4. Tasks required to examine parts or the whole body of machines or equipment and to test their operations."

These jobs can be found in places where dozens of human hands have been replaced through advanced mechanization and automation, as in power stations, oil refineries, railway dispatching centers, airports, and radar control stations, where work has to be carried out continuously throughout the day and night.

Another category of jobs is those demanding manual skill, but little physical effort. In monotonous manual work, the motor activity of a worker is often reduced to stereotype movements that are so simple they can be done almost without any visual or conscious mental control. Such activity is sometimes very tiresome because of the monotony of the surroundings and the boredom of continuously performing identical operations, making continuous attention to the performed tasks difficult.

Some authors (22,246) have seen that shift workers participating in mental or repetitive work, adapt themselves to night work with greater difficulty than those engaged in physical work. Therefore, people performing such jobs have to fight sleepiness throughout the whole night shift and all vigilance tasks are for them more difficult than in the daytime. Particularly, the tasks performed under conditions of relative perceptual isolation or monotonous surroundings intensify the sleepiness. Physical work, if light and of short-duration, can improve mental performance by raising the level of arousal (59). Therefore, interrupting continuous tracking tasks with short periods of light physical work can improve mental performance; especially at night, when the level of arousal is low.

It is incomparably more difficult to study the psychological and neurophysiological functions involved in mental or sensory-motor performance than to estimate the physiological functions of physical work. The methods used to study the former are so limited that the conclusions

Preceding page blank

refer usually to the performance itself (its improvement or impairment), rather than to mechanisms. Theoretically, actual work performance could be estimated by measurements of work efficiency, but the comparison of efficiency on various shifts would be justified only under identical working conditions. However, it is known that conditions often differ. Sometimes better conditions of work are observed on night shifts than on day shifts when the workers are more often distracted from their job. And in such situations, where the performance is assessed in measurable quantities, the performance "on the job" may be a quantitative criterion only. Nevertheless, the question is how to measure the productive output, for instance, of an operator or pilot. In the case of physical work, not only the output, but parallel physiological functions can be quantitatively assessed allowing the evaluation of efficiency and physiological load. But how can the "psychological load" on an operator be estimated?

For the reasons discussed above, the results of studies referring to day-night variations will be presented in a descriptive manner. Generally, most observations point to a decrease of mental and sensory-motor performance at night. The poorest performance is usually obtained in the early morning. Attention is also drawn (46,98, 142) to the existence of an additional decline of general psychomotor performance in the afternoon hours (post-lunch dip). This short impairment of performance also can be observed even if a meal is not consumed. Contrary to the lessened activity at night, the post-lunch dip is not accompanied by a decrease in the body temperature. Usually, the post-lunch dip does not exert a great influence on work performance because it coincides with the end of the morning and the beginning of the afternoon shift.

Depressed mental performance during the night hours may be related not only to the circadian rhythms but, also, to sleep deprivation (35,79,111). The influence of the sleep deprivation is difficult to eliminate because of the "poor" sleep experienced in the daytime. When reporting for night duty, the shift workers are often already tired and sleepy. This should not be overlooked when analysis of experimental results is undertaken. (See Chapter V.)

One of the tests commonly used in studies of fatique depends on the assessment of flicker fusion frequency. When work is performed continuously throughout many hours, the critical fusion frequency of flicker decreases. Such changes were seen especially during (or after) night work (21,99,100,144,145), along with circadian change in reaction time. Both simple reaction time (the time lag between the onset of the signal and the onset of the response) and choice reaction time (different stimuli calling for different responses) are usually prolonged at night (12,13, 42,89,91,135,144,172, 173,220,253,262). The highest and lowest values usually have been observed soon after midnight and in the afternoon, respectively. In the experimental studies of Klein, Wegmann, and Bruner (135), the increased reaction time at night coincided with the decline of individual variance of the reaction time (fig. 22),

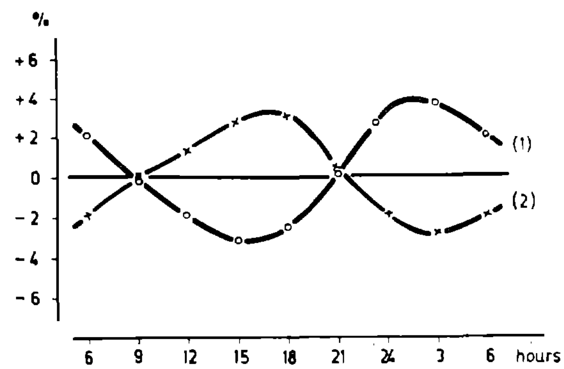


Figure 22. Circadian rhythm of (1) reaction time and (2) individual variance of reaction time. The values were averaged "vertically" to a mean 24-hour cycle for the total group of 17 subjects (Klein, Wegmann, and Bruner, 1968).

which would seem to contradict the concept that the "steadiness" of mental performance is best in daytime. However, these studies did not note significant statistical differences for the reaction time and its standard deviation.

Barhad and Pafnote (21,22) estimated that the reaction time of shift workers was longer at the beginning of the night and afternoon shift than of the morning shift. The authors related these findings not only to the circadian rhythm of performance, but also to the fatigue resulting from the work performed before arriving at the factory. In fact, the longer reaction time for the night shift seemed to be the result of interaction of the circadian rhythm and loss of sleep.

The prolongation of the "psychological refractory period" at night may be the cause of the decline of work efficiency of those cases in which the efficiency depends upon the rapidity of answers to the stimuli. Measurements of reaction time during work performance are only possible in a situation in which rapid reaction to the signals is an element of the work itself, thus, avoiding interrupted work. A study of teleprinter operators by Browne (34) measured the delays in answering teleprinters' calls during shift work. The length of time between onset of the stimulus (the signal light) and the onset of the response (i.e., lifting of the receiver) was measured. It appeared that the delays in responses were considerably greater during night shifts (fig. 23).

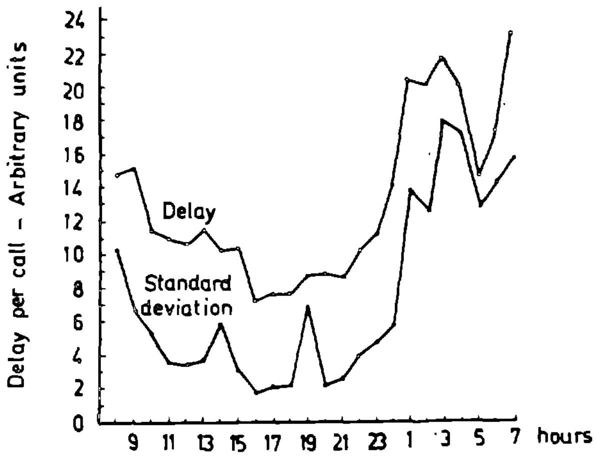


Figure 23. Delay in answering the calls by teleprinter switch-board operators during their shift work (Browne, 1949).

Also, circadian changes in the standard deviation paralleled the changes in delays, in contrast to the previously described findings of Klein, Wegmann, and Bruner (135).

One of the possible causes of poor performance at night where visual control is necessary, seems to be connected with day-night variations in visual perception. It is known that the visual perception time is prolonged at night and the threshold of sensitivity to auditory stimuli (for air conduction) is higher. The same refers to the threshold to sensory electrical stimuli and to the optic rheobase (21,22,91,170,193,276). In our own studies (Makowska and Wojtczak-Jaroszowa, 170), the visual perception time and sensitivity threshold to auditory stimuli were determined in students and workers during the day (between 9 a.m. and 1 p.m.) and at night (between midnight and 4 a.m.). After familarization with the procedure of the experiment, meaningless three letter syllables were displayed by a tachistoscope. The period of display was increased until the time for correct reading was attained. The sensitivity threshold to auditory stimuli was studied by gradual lowering of the stimuli (for air conduction). To secure the same period of wakefulness before both day and night experiments, the subjects slept during the afternoon before the night experiments. Small but highly significant statistical differences were noted between the results of day and night sessions. Namely, the time necessary for correct reading of syllables was significantly longer, and the threshold for auditory stimuli was significantly higher, at night (for both, $p<0.001$). The differences were especially pronounced for the high frequency tones.

Irrespective of the causes of these differences, the elevated threshold of sensitivity to the stimuli at night can influence work efficiency. In fact, perception plays an important role in all inspection tasks. It is possible that circadian changes in performance observed by Bjerner, Holm, and Swensson in gas workers could have been related, at least to some degree, to the changes in visual perception (28,29). The workers' performance depended on controlling the instruments which registered the consumption of gas, its pressure, and other parameters. The data collected included errors in the figures, both in noting the readings from the instruments and in calculations. It appeared (fig. 24) that the occurrence of errors made by the workers varied with the maximum during the night shift and the minimum during the morning shift.

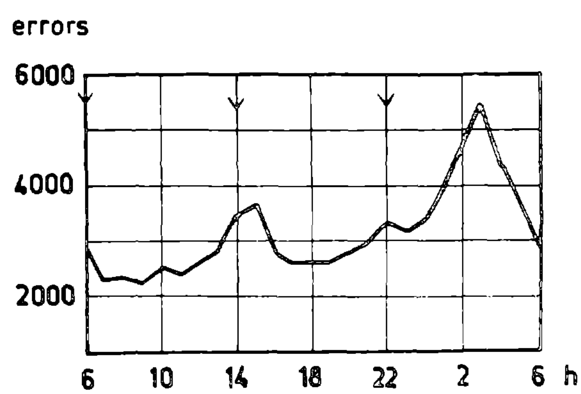


Figure 24. Distribution of errors during the shift work of gasworkers (Bjerner and Swensson, 1953).

Reduced efficiency due to more errors or slower work speed is a usual, but not the most severe, consequence of lower sensory-motor performance at night. In numerous occupations, for instance in airline pilots, drivers, and engineers even the slighest error can present a direct and immediate danger to life. Lower ability to perform the work correctly in vigilance situations may lead to greater frequency of accidents at night, as noted by some authors (56,181). Klein et al. (134), during their studies on pilots, were able to show that flight risk was greater at night than during the day. The studies were conducted in a supersonic flight simulator at various times of the day and demonstrated that the time required to make the necessary readjustments to the correct position after occurrence of a stimulated flight incident was longer at night. A deviation from the pre-set range, speed, and altitude of flight occurred more often at night than during the day (fig. 25).

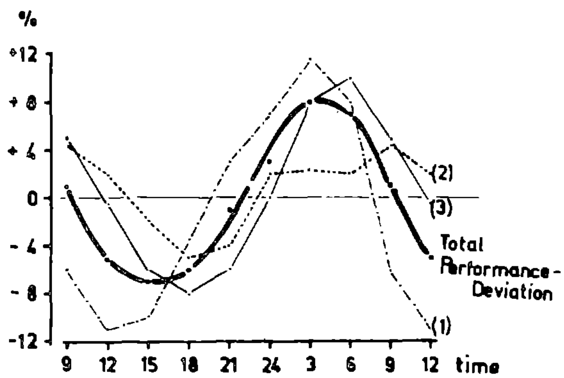


Figure 25. Circadian rhythms for the performance of 14 pilots during standardized simulator flights: deviation from a (1) given range, (2) speed, and (3) altitude, in percent of the 24-hour average (Klein et al., 1970.)

A night time "dip" in human performance has been revealed by numerous studies using a variety of tests including calculation tests, memory tests, tracking, and vigilance tasks (47,48,49,50, 81,136,181,267). In the studies of Jansen, Rutenfranz, and Singer (122), the best performance was observed between 6 p.m. and 10 p.m. in tracking tasks, and between 10 a.m. and 2 p.m. in calculation tests. However, under conditions of a stabilized night shift system, in which the hours of work and rest are the same each day, a clear improvement of performance in calculation (simple summation) and vigilance tests were observed on successive nights (40). This improvement in performance at night occurred earlier than did the changes in the daily body temperature rhythm.

A decline in performance at night occurs more frequently for complicated tasks, such as the tracking task with simultaneous adding of two digit numbers (122). In our studies of glass factory workers (Rzepecki and Wojtczak-Jaroszowa, 221), the Toulouse-Pieron figure cancellation test (in our own modification) was used. The work, manual cutting of the glass-plate, required a high degree of accuracy and precision of movements. Observations were made on the same workers three times during each shift (at the beginning, after 4 hours of work, and at the end of the shift) on the morning (6 a.m. to 2 p.m.), afternoon (2 p.m. to 10 p.m.), and night (10 p.m. to 6 a.m.) shifts. During each experiment, the first task was a page with different numerals in which the subject had to recognize and cross out all of three different specified numbers. Directly after the first task, each person was given a second task with reversed orders to cross out the other three figures, which had not been eliminated in the first task. Thus, the figures which caused "positive" reactions in the first task formed "inhibitory" stimuli in the second. The experimental situation required learning a new response for the signals which had a different meaning in the two situations. The subjects were instructed to perform the tasks as quickly and accurately as possible, crossing out all the three figures on the page, beginning at the first line, working from left to right, and continuously down the page through the subsequent lines of numbers. For each task (both the first and second), the working time was limited to one minute. The workers were familiarized with the experimental procedure and had considerable practice on the tests. In analysis of the data, the number of figures checked during one minute and the number of errors were used.

The performance was poorer after 4 and 8 hours of work than at the beginning of every shift (fig. 26). This was particularly evident during the

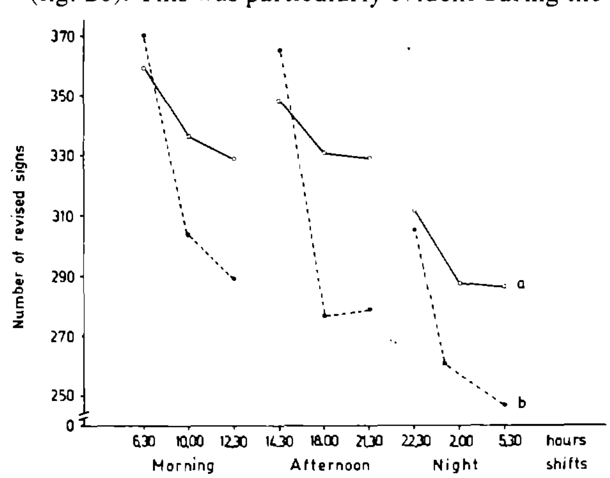


Figure 26. The changes in results of Toulouse-Pieron test which was performed by 10 glassworkers during shift work: (a) first task and (b) second task. The test was repeated three times during every shift: at the beginning, after 4 hours, and at the end of the work (Rzepecki and Wojtczak-Jaroszowa, 1969).

night shift. These differences were seen as well in the first (a), as in the second (b), task. But generally, the second task was much more difficult to perform than the first one. The negative influence of the first task upon the second resulted mainly from a considerably lower speed of performance and resulted in a reduction of the amount of performed work, i.e., in a decrease of the number of figures checked in one minute (p= 0.033 and p= 0.036, when the results of night experiments were compared with those obtained during morning and afternoon shifts, respectively).

The experimental scheme simulated real life by requiring a change in a "known" stimulus. In these experiments, learning the first task made learning the second one more difficult. This was manifested especially during the night shift, and after many hours of continuous work. It is likely that under influence of various asthenizing factors (as fatique, sleep deprivation, or emotional stress) the previously established behavior manifests itself and overrides the more recently trained reaction patterns. It seems also possible that at night (due to low level of arousal) the inhibition may be more pronounced than in the daytime.

A majority of tests used by various authors involve, to some degree, motor activity. Generally, in all tests for which the subject is instructed to perform a motor reaction in response to a given stimulus, the results depend considerably upon manual skill and the speed of movements. Results of tests in which visual control is minimal seem to suggest that the reduction in performance at night may result from a decline in manual performance (Makowska and Wojtczak-Jaroszowa, 169). When such tests are used, lower scores at night result. The tasks used in our studies (tapping test and finger ergograph test) were so simple that they did not require visual control. The subjects were asked to perform the tasks at the maximum possible rate. The experiments were carried out during the day (between 9 a.m. and 1 p.m.) and at night (between midnight and 4 a.m.). The speed of tapping and the output of ergograph test were significantly lower at night than in the daytime (p= 0.001 and p= 0.02, respectively), but no day-night difference was found when the subjects were asked to tap at their most preferred rate. This is not in agreement with the results of Aschoff et al. (13), who observed circadian variations when tapping was performed at maximal, as well as, in preferred tempo.

It is also worthwhile noting that at night, apart from the lower speed of movements during tapping, an irregular tempo was also recorded as breaks in tapping were observed from time to time (fig. 27). The subjects were usually conscious

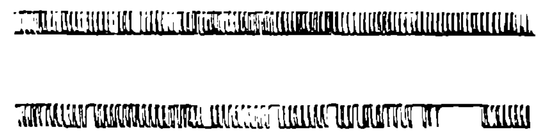


Figure 27. Fragment of a record from the 3-minute tapping test: (a) in the day at about 10:30 a.m. and (b) at night at about 3 a.m. Tapping was performed at maximal speed (Makowska and Wojtczak-Jaroszowa, 1971).

of these breaks, but claimed they were not able to maintain a constant and uninterrupted rhythm of tapping at a rapid rate.

Persuasive data referring to day-night variations in manual performance have been provided from our studies performed on female spinners while at work (Wojtczak-Jaroszowa and Pawlowska-Skyba, 285). Throughout the entire shift, the time spent per work unit (joining the broken threads) was noted. The studies were made on the same subjects during morning (5:30 a.m. to 1:30 p.m.), afternoon (1:30 p.m. to 9:30 p.m.), and night (9:30 p.m. to 5:30 a.m.) shifts. The workers selected for this study had been on shift work for at least 10 years. They performed their work with great proficiency and with minimal visual control. It was shown (Table 4) that the time required per work unit was significantly longer at night than in the morning (p= 0.006). Changes of work efficiency during each shift show that (fig. 28) the rate of work was minimal at about 3 a.m. and maximal between 8 a.m. and 11 p.m.

Thus, even simple manual tasks took longer to do at night than in the daytime. In our studies (169,221,276,285), the difference between the results of day and night experiments amounted to about 10 percent. This difference was revealed in standardized experimental situations, as well as under occupational conditions, and was seen not only in subjects who worked days only, but also in workers with long experience on shift work. The question, in the case of manual work, is whether the required rate of performance should be the same for both day and night shifts. A rate of work which is satisfactory for the day shift might be too high for the night shift.

Causes of day-night variations in manual performance can probably be found in some neuromuscular changes. The genesis of these

TABLE 4

SHIFTS					
Morning		Afternoon		Night	
Hours	% (sec)	Hours	% (sec)	Hours	% (sec)
5:30-6:30	0.98 (6.06)	13:30-14:30	1.00 (6.23)	21:30-22:30	1.05 (6.38)
6:30-7:30	0.91 (5.62)	14:30-15:30	0.93 (5.68)	22:30-23:30	1.00 (6.13)
7:30-8:30	0.90 (5.53)	15:30-16:30	0.93 (5.67)	23:30-24:30	1.09 (6.73)
8:30-9:30	0.93 (5.73)	16:30-17:30	0.95 (5.86)	24:30-1:30	1.06 (6.51)
9:30-10:30	0.90 (5.47)	17:30-18:30	0.92 (5.58)	1:30-2:30	1.08 (6.60)
10:30-11:30	0.95 (5.82)	18:30-19:30	0.99 (6.11)	2:30-3:30	1.13 (6.91)
11:30-12:30	0.99 (6.09)	19:30-20:30	1.10 (6.85)	3:30-4:30	1.05 (6.47)
12:30-13:30	1.01 (6.22)	20:30-21:30	1.08 (6.68)	4:30-5:30	1.03 (6.27)

Table 4. Average time (in percentage) of work unit (5 female spinners) during morning (5:30 a.m. to 1:30 p.m.), afternoon (1:30 p.m. to 9:30 p.m.), and night (9:30 p.m. to 5:30 a.m.) shifts. The measurements were performed throughout every shift hour by hour. The percentage was calculated individually taking the mean value of all measurements as 100 percent. In parentheses the absolute values in seconds are noted. About 5,000 measurements were recorded (285).

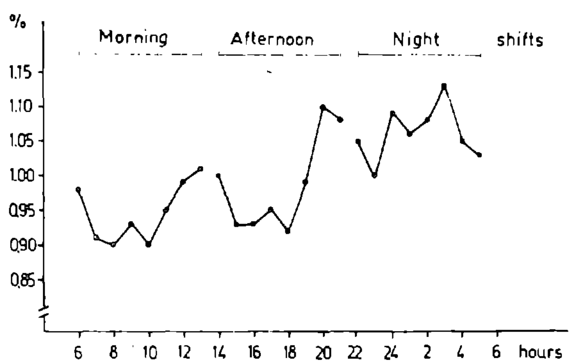


Figure 28. Changes in work efficiency (time per work unit in percentage) of five spinners. The percentage values were calculated individually, taking the mean values of all measurements as 100 percent (Wojtczak-Jaroszowa and Pawlowska-Skyba, 1967).

changes is discussed in a report of our recent electromyographic studies (282). The electromyographic activity of forearm flexor muscles was recorded during voluntary pressing on a button. The surface electrodes used were fixed at the points proposed by Lippold (160). The initial period of electrical activity (IPe) was analyzed and defined as the time elapsing between the onset of electrical activity in the EMG (the point at which the action potential spike first leaves the baseline) and the initiation of the mechanical event (281). Studies were made on 31 healthy subjects (without neurological disturbances) who usually worked the day shift and who were familiar with the experimental procedure. The examinations were performed several times during the day, between 10 a.m. and noon, and at night, between 1 a.m. and 3 a.m.

Preliminary analysis (Table 5) revealed that the length of IPe was significantly longer at night ($p = 0.001$). To obtain a better insight into the nature of these differences, a detailed analysis was made of more than 300 EMG records on six subjects randomly selected from the group. For this purpose, the area of the region determined by the EMG curve in IPe was measured in successive 10 msec intervals. Then, three functions denoted by A,B, and C were calculated for IPe:

$$A(t) = \int_a^t |f(x)| dx \quad (2)$$

where $a < t < b$, and where "a" is the point of first incline of the EMG curve from the baseline, "b" corresponds to the onset of mechanical events, and "f" is the function of the voltage in the course

TABLE 5

Subject	$\frac{x_2 - x_1}{x_1} \times 100$	Subject	$\frac{x_2 - x_1}{x_1} \times 100$	Subject	$\frac{x_2 - x_1}{x_1} \times 100$
1.	+14.4	11.	−37.0	21.	+30.3
2.	+11.8	12.	+18.6	22.	+6.2
3.	+41.6	13.	+14.5	23.	+58.2
4.	+20.1	14.	−0.3	24.	+101.3
5.	+27.0	15.	+59.8	25.	+147.4
6.	+12.6	16.	+154.5	26.	+12.9
7.	+2.9	17.	+28.8	27.	+4.9
8.	+34.8	18.	+44.3	28.	+36.5
9.	+71.4	19.	+44.9	29.	+18.4
10.	+46.2	20.	−5.5	30.	−36.1
				31.	−41.5

Table 5. The differences in length of IPe between day (x_1) and night (x_2) experiments (31 subjects). The experiments were performed between 10 a.m. and noon, and between 1 a.m. and 3 a.m. taking the day values as 100 percent (282).

of time from point "a" to point "b". Thus, for each "t", A(t) is the area of the region determined by the graph of the function f from "a" to "t".

$$B(t) = \frac{A(t)}{t - a} \qquad (3)$$

where $a < t < b$. This function has been interpreted as a function of the mean velocity of the increase of surface under the graph "f". It was called the function of "mean amplitude."

C function, was obtained by linear interpolation of the integrated mean of function "f" in successive intervals of 10 msec duration.

The curves of all three functions were clearly different for day and night sessions. The curves of function C are presented on figure 29a. In day experiments, the mechanical response appeared at 110 msec from the first point of decline of the EMG curve from the baseline. At night, the length of IPe was longer and the mechanical response appeared at about 170 msec after the first potential. The regression lines corresponding to function B (fig. 29b) clearly demonstrate the development of bioelectrical events during IPe. The inclinations of these lines were different for the day and night experiments with the slope of the line for night experiments being less steep than for the day ($p = 0.008$).

The IPe corresponds to the initiation of recruitment of motor units before the mechanical event. At the end of the recruitment period, the number of activated motor units and the frequency of their discharges becomes sufficient for the onset of the mechanical event. The presented results suggest that activation of motor units during IPe occurs more "dynamically" in the daytime than at night. The slower recruitment of motor units, preceding the mechanical event, could be responsible for the lower speed of manual performance at night as described previously.

The mechanisms underlying the lower efficiency of electrical activity at night seem to be similar to those which are responsible for day-night variations in the latency period of motor responses as described by Wyrwick and Duncan (288). Possibly, some biochemical changes occurring in contractile material during the contraction of the muscle could be the cause of the observed variations. It is also possible that the recruitment of motor units might be centrally limited at night.

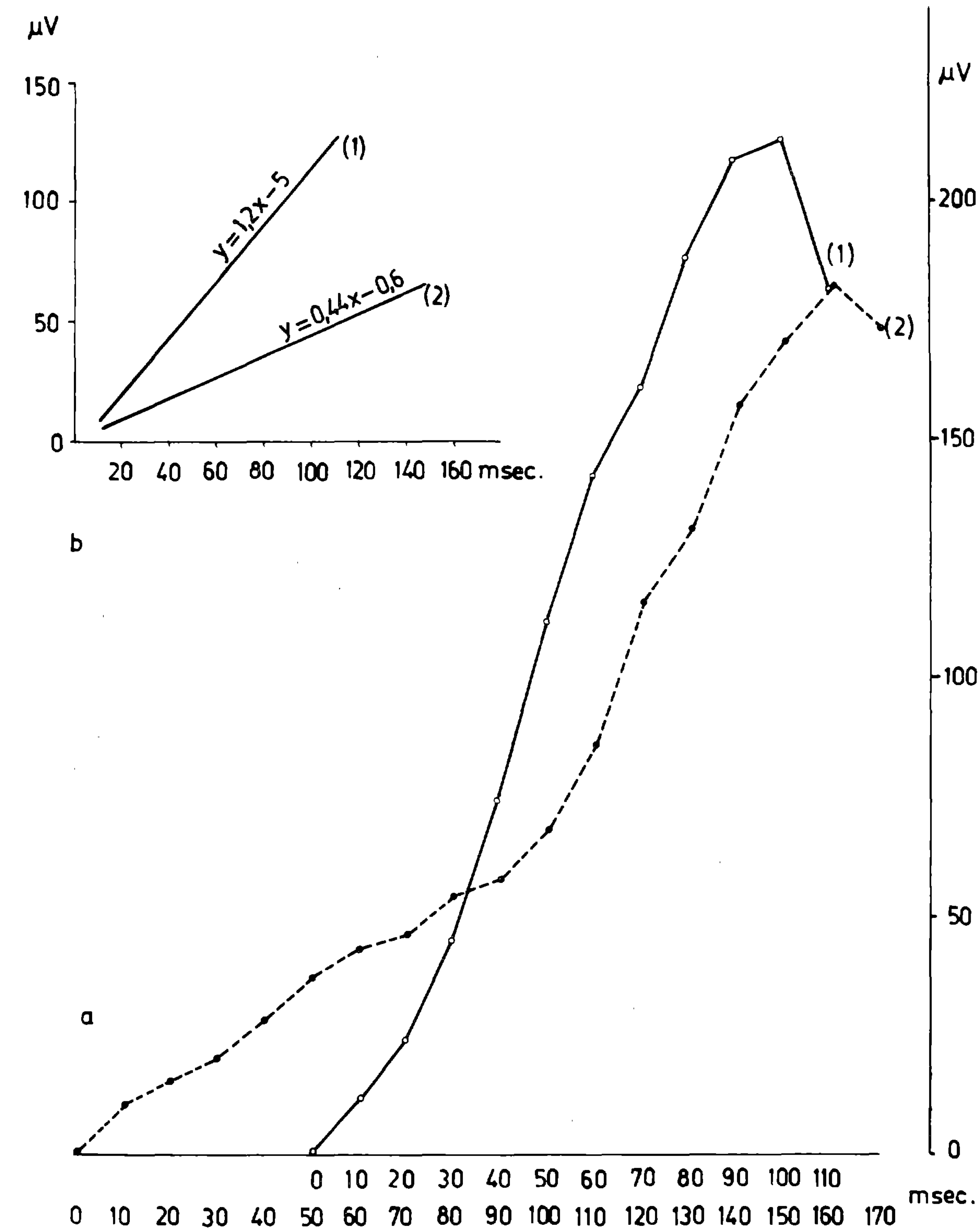


Figure 29. The curves of (a) "integrated amplitude" and (b) the regression lines of "mean amplitude" during the initial period of electrical activity (IPe) of the muscle. The measurements were performed (1) between 10 a.m. and noon, and (2) between 1 a.m. and 3 a.m. (Wojtczak-Jaroszowa, Maciaszek, Jarosz, 1975).

CHAPTER IV

DAY-NIGHT VARIATIONS IN PHYSIOLOGICAL RESPONSES TO HEAT STRESS

In numerous branches of industry, shift work is done under hot environmental conditions. The technology of the process often does not allow interruption of production, and the work has to be done continuously, involving a night shift. Therefore, it is important to know whether human tolerance to heat stress is the same during the day as at night. Data from several studies indicate a circadian variation in thermoregulatory behavior (116,183,211). Nevertheless, the same criteria are used for the assessment of heat load during the day as at night without any evidence in the available literature to support this position.

Although industrial situations are not included in the few references to day-night variations in response to heat exposure, some of the variations will be discussed in terms of their importance in shift work.

First of all, not only the deep body temperature, but also skin temperature (fig. 30) displays a regular circadian rhythm (8,14,100,113). According to most of the data, the circadian rhythm of the skin temperature of the extremities is a mirror image of the rhythm of deep body temperature. Bloch (30) reported that the maximum and minimum skin temperatures of the extremities were reached between 8 p.m. and 4 a.m. and between 8 a.m. and 4 p.m., respectively. These rhythmic changes in skin temperatures are not related to variations in ambient temperature and are observed when the subjects are resting in bed, as well as, when they are ambulatory during the day. It is impossible to explain the internal body temperature's rapid morning rise and low ebb at night without reference to the circadian variation of skin temperature of the extremities.

According to Geschickter, Andrews, and Bullard (94), night skin temperature increased about half an hour before the onset of sleep and about 90 percent of the total sweat loss, occurring during the night sleep period, took place prior to the minimum deep body temperature. This could suggest that the decline of body temperature during the night is connected with greater sweat production. It is remarkable, however, that in the same subjects no decrease in body temperature had been observed during afternoon naps, in spite of a concurrent increase in sweat production.

Contemporary views (Aschoff, 14) hold that regular variations in skin temperature of the extremities is the principal factor determining the circadian periodicity of deep body temperature. The increase of heat loss from distal parts of extremities during the night would be responsible for the decline of deep body temperature (fig. 31). Day-night variations of the internal conductance* also have been observed (fig. 32). Those variations are related to changes in blood flow through the extremities (226,234) and could be the basis for circadian variations of body temperature regulation.

Interesting data on circadian rhythm in physiological responses to heat loads have been provided by Little and Rummel (161). They observed eight healthy men subjected to one hour heat exposure in a heat chamber, where the environmental parameters were kept constant at 46°C T_a and 31 percent relative humidity (rh). The experiments were repeated at different times of the day, i.e., at 4 a.m., 8 a.m., noon, 4 p.m., 8 p.m., and at midnight, on several days. The subjects reclined during the experiments and no

---

* The coefficient for internal conductance of the whole body is obtained by dividing the total heat loss from the body's surface by the difference between core temperature and skin temperature (12).

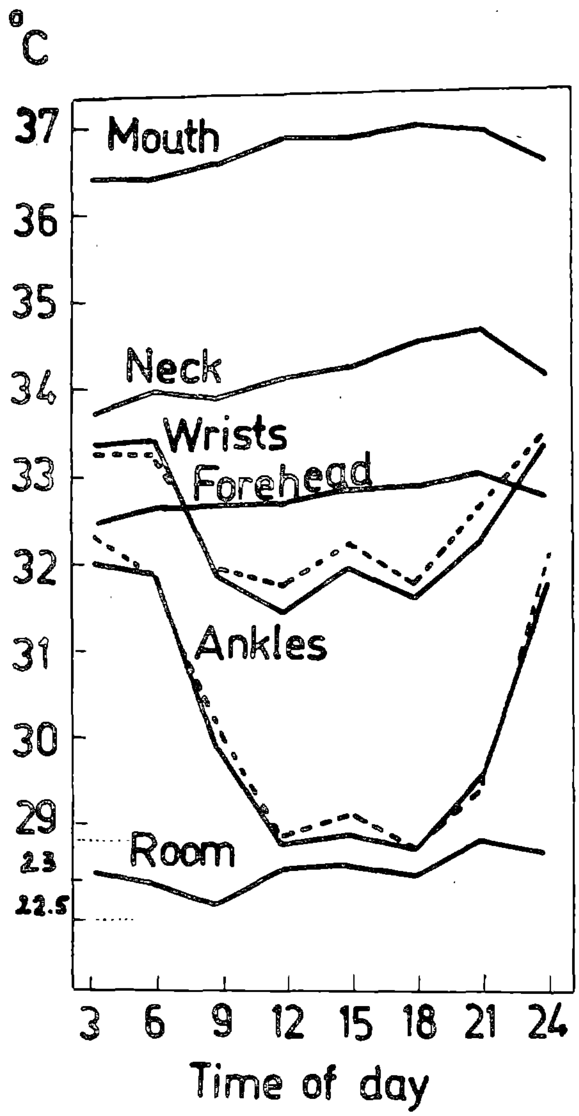


Figure 30. Variations in the temperature of different areas of the body at various times of the day (Heiser and Cohen, 1933).

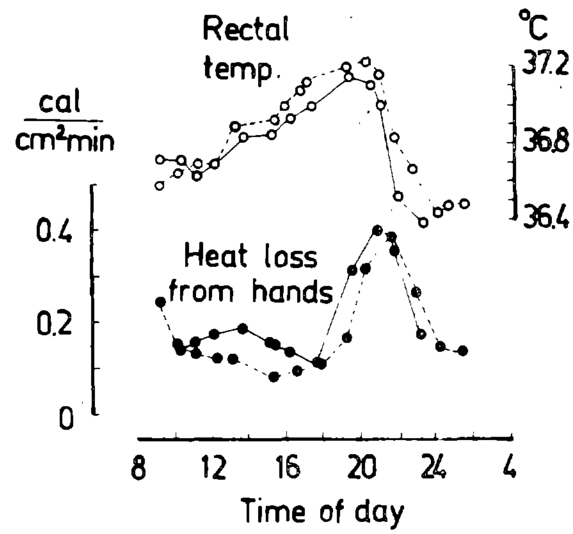


Figure 31. Rectal temperature and heat loss from hands (in running water of 32°C) as a function of the time of day. During the experiment the subject was fasting and sitting comfortably at an ambient temperature of 24°C (Aschoff, 1955b).

physical work was performed. For 30 minutes prior to the heat test, the subjects rested on a cot at a room temperature of 24°C T_a and 50 percent rh. After the parameters characterizing physiological strain from heat exposure were compared with those recorded prior to the test, clear circadian variations in sweat loss were noted (fig. 33). The rate of sweating increased throughout the afternoon, reaching its peak at about 8 p.m., whereas its minimum was observed at noon.

Circadian rhythmicity was also noted in regard to rectal and skin temperature, heart rate, and metabolic rate at room temperatures, as well as, under heat stress. However, in the hot environments, the rectal and mean weighted skin temperature 24-hour cycle amplitudes were reduced (figs. 34,35). Apparently, in spite of greater sweat loss at night, the rise of body temperature (above the level estimated prior to the heat exposure) was greater at night than during the day. It is interesting that the smallest increase of rectal temperature under the influence of heat exposure occurred during the day when the sweat rate was lowest. In contrast, the higher values of both sweat loss and the increase of rectal temperature were recorded in the afternoon and at night. Summarizing, the physiological strain in man exposed to a given heat load varies throughout the day with some physiological responses being more pronounced in the afternoon and at night than during the daytime.

The data are not sufficient to state conclusively whether or not the harmful effects resulting from work in hot environments could also depend upon the time of the day or night during which the heat exposure took place. However, in light of the discussed findings on day-night variations in human tolerance to heat stress, especially in the cases of more severe and/or prolonged exposure, the permissable exposure time to heat stress should be set differently for the day and the night shift. Also the day-night variations in physiological responses to heat stress should be considered when threshold limit values are established. These and many similar questions are of great importance for industries where heat stress is still unavoidable.

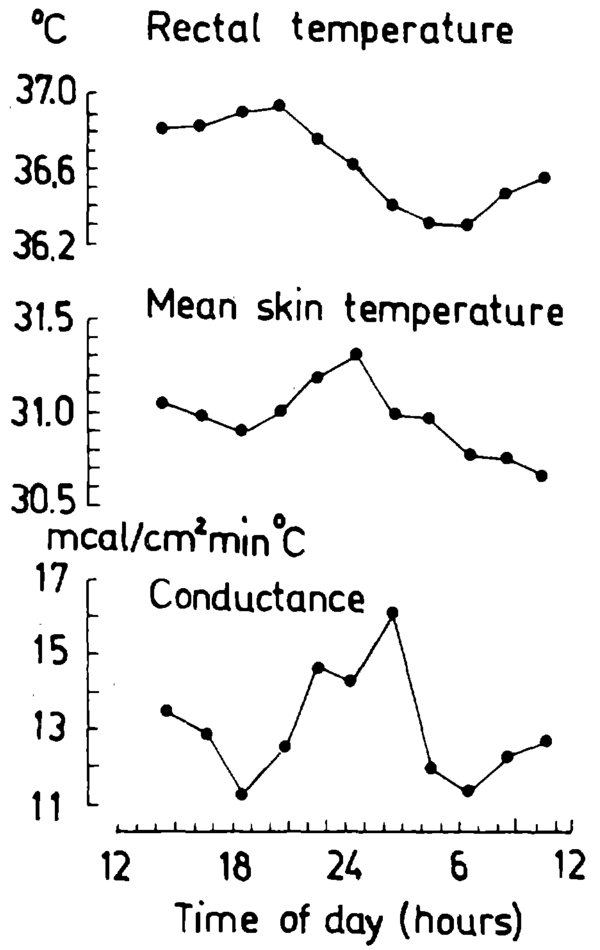


Figure 32. Rectal temperature, mean skin temperature, and internal conductance (core to skin) as a function of the time of day. Average data from six subjects, resting nude in an ambient temperature of 20°C (Aschoff, 1972).

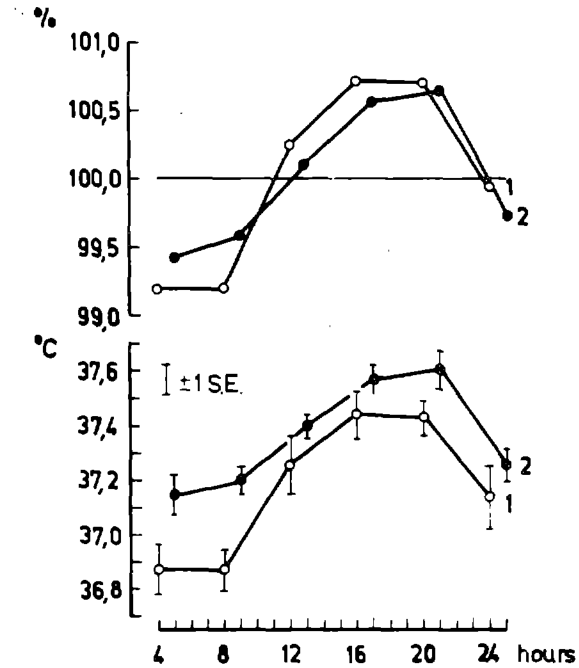


Figure 34. Mean 24-hour variations in rectal temperature of eight subjects (1) before and (2) at the 60th minute of heat exposure. Values are expressed in absolute terms (°C ± 1 standard error) in the lower graph and as percentages of 24-hour means in the upper graph (Little and Rummel, 1971)

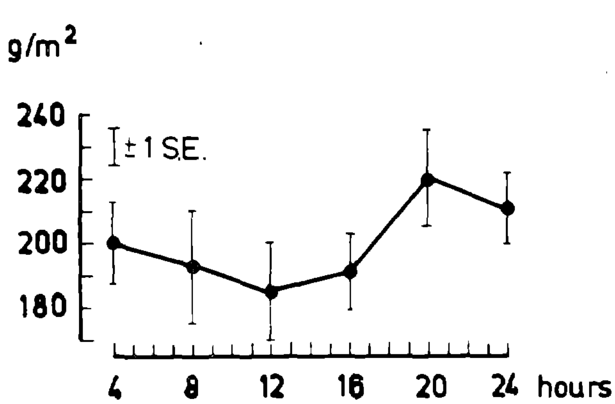


Figure 33. Mean 24-hour variations in the water loss of eight subjects after 60 minutes of exposure to heat (Little and Rummel, 1971).

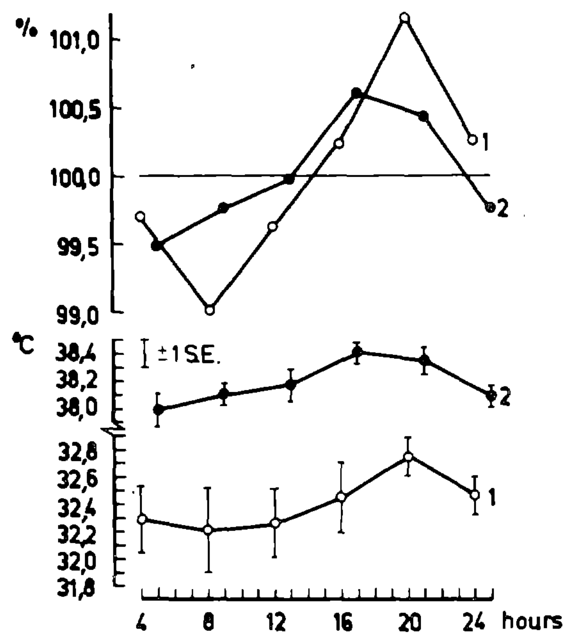


Figure 35. Mean 24-hour variations in mean weighted skin temperature eight subjects (1) before and (2) at the 60th minute of heat exposure. Values are expressed in absolute terms (°C ± 1 SE) in the lower graph and as percentages of 24-hour means in the upper graph (Little and Rummel, 1971).

CHAPTER V

IMPORTANCE OF SLEEP AND REST FOR SHIFT WORKERS

"All men sleep. Between the darkness out of which we are born and that in which we end, there is a tide of darkness that ebbs and flows each day of our lives. A third of life is spent in sleep, that profoundly mysterious sovereign to which we irresistibly submit, lying almost immobile for hours, removed from the waking world."

— *G.G. Luce and J. Segal*

According to the terminology of Pavlov's school, the inhibitory processes predominate in the cerebral cortex during the night even in individuals who have been employed on the shift system for many years (21,87,91). Impaired ability to differentiate and delayed response in conditioned reflex behavior have been observed at night. Babadzhanyan and Muksinova (17) claim that the rhythmic succession of excitation and inhibition in man, related to the natural alternating periods of light and darkness, had evolved phylogenetically. According to this hypothesis, sleep is a reaction to darkness and depends upon the radiating of the inhibitory process over the cerebral cortex. This might explain why it is so difficult to overcome sleepiness.

As a rule for shift workers, the length of sleep is longest when they work in the afternoon and shortest when they work at night. Night shift workers living under "poor" housing conditions often cannot sleep more than 3 to 4 hours per day, which is inadequate for full recovery. However, it is difficult to say how much sleep is necessary. Young adults sleep 7.5 to 8.5 hours per day although considerable individual variation has been observed (177,263). Prior to contemporary medical knowledge, 8 hours of sleep was thought necessary for the normal functioning human. In the 12th century, the philosopher Maimonides proclaimed: "The day and night is 24 hours. It is enough for men to sleep one third of them" (165).

Full restoration after a work shift depends on the organization of the worker's off-time. Appropriate use of this time is especially important when the worker is on the afternoon or night shifts. On these shifts the time preceding the work is often used for other activities. Studies show that at the beginning of the night or afternoon shift, the workers are already tired from non-occupational activity (21,91,97,197). Skilled technicians often use their free time to earn extra money (205), and workers who have large families usually spend a lot of time on household duties, which makes recovery for work difficult. As a result, the workers arrive at the factory having already spent many hours working, sometimes more strenuously than at their regular occupational job.

Day sleep after night duty coincides with the activity of the worker's family. Social conditions (social "timegivers") are most apparent among numerous factors which are considered as exogenous synchronizers. Consciousness of what is happening, what other members of the family and neighbors are doing, disturb the worker's day sleep.

Most often, housing and family conditions make the proper organization of rest after night duty difficult. From an analysis of the causes of disturbed sleep, it appears that noise is most common. Highest among the complaints, is the noise of street traffic, passing trains, conversations, water pipes, radio and TV, children at play, factory noise, etc. (1,74,143,219,247). On the other hand, whether it is light or dark during sleep is of relatively little importance. An uninterrupted and sufficiently long day sleep is a first requisite for tolerance to the night shift. Also, no adaptation to the night shift can be seriously considered if there is no opportunity for adequate rest during the daytime. It is emphasized very often that not only the shift worker, but also members of his family, must understand the importance of the allocation of a sufficiently long sleep. Therefore, whether the worker is tired and sleepy or sufficiently recovered before working on the night shift depends largely on the consideration of the family.

Attempts had been made to solve the problem of sleeping after night duty by providing in factories special bedrooms, well insulated from noise, (88,203,208). However, this solution has not been accepted by most workers because it meant isolation from families and social life while on the night shift. Presently, emphasis is largely on the design of houses for shift workers; adequately sized flats and the appropriate location of bedrooms that would insure satisfactory relaxation during day hours. It has been pointed out that optimal housing conditions for rest during the day should be investigated before a worker commences shift work (23,37,207,243,249).

Complaints related to sleep are well known to physicians employed in factories where a majority of the workers are on a shift system. The complaints include difficulties in falling asleep, waking episodes during the sleep period, sleeplessness and overly light sleep, and being easily disturbed by a mild noise (100,244,254). However, even with good housing, shift workers often have "poor" sleep after night duty and, in spite of their tiredness, sometimes are not able to fall asleep. Similar psychophysiological problems accompanied by sleep disturbances have been reported in aircraft crews and passengers during long journeys involving rapid time zone translocation. These symptoms, called "travel or jet fatigue," are not related to the alterations of the circadian rhythms of biological functions (36,43,194), but rather that they are out of phase with real time.

Sleep disturbances appear in young subjects as well as in older workers who had been employed for a long time on shift work. According to some data (168), the complaints about sleep disturbances are sometimes even more frequent among older workers. This observation counters the theory that adaptation to night work occurs during long periods of participation in a shift system. It is also noted that during trans-Atlantic flights, older people adapted their sleep-wake cycle with difficulty to a new time zone (72). According to Picrach (203), the appearance of sleep disturbances in people who tolerated night work for many years, should be treated as one of the signs of incipient arteriosclerosis of the cerebral vessels.

Electroencephalographic (EEG) sleep analysis has shed some light on the mechanisms of these disturbances. It is presently recognized that sleep is not a state of uniform pattern in which there is "nothing happening." "The process of sleep as revealed by the EEG, is a complex and dynamic one rather than a simple drifting into sleep and lying awash in the gentle tides of the night" (264). It is possible not only to recognize the difference between sleep and wakefulness, but also to assess the depth of sleep. During the period of wakefulness (Stage O) the alpha activity of 8 to 12 cps waves dominate in the EEG. In the period corresponding to drowsiness and falling asleep (Stage 1), these waves disappear and are replaced by relatively low voltage, mixed-frequency waves with "spindling." Stage 2 sleep is identified by the bursts of 12 to 14 cps regular waves ("sleep spindles") and/or k-complexes (sharp negative waves which are immediately followed by a positive component). In Stage 3, at least 20 percent, but less than 50 percent, of the record is occupied by the relatively high voltage waves of 2 cps, or slower. In Stage 4, the deepest physiological sleep, there is 50 percent or more of high-voltage slow waves. During this phase, the non-rapid eye movements (NREM) can be observed, whereas dreams* are often accompanied by rapid eye movements (REM). The EEG of REM sleep corresponds to that of Stage 1. During normal night sleep, lasting about 7.5 hours, the REM sleep makes up 20 to 25 percent of the total sleep time.

In a detailed analysis of sleep pattern, the following features are most often taken into account: the total length of sleep, temporal distribution, and the amounts of Stage 4 and Stage REM.

Sleep shows its own biorhythm with regard to Stage 4 and Stage REM. During normal night sleep, Stage 4 dominates in the first one-third of the night, whereas Stage REM occupies a greater proportion of time later in the night. It has been noted also that REM episodes occur at rather regular intervals of about 90 minutes. Thus, there are four to five episodes of REM during 7.5 hours of sleep. Webb (264) describes the pattern of sleep.

---

* According to some concepts, dreams occur in all stages, and are not restricted only to REM sleep. (124).

Sleep pattern is clearly affected by age (fig. 36; 127,157,164,263). The sleep of children and young people shows infrequent awakenings, whereas elderly people often awake several times during the night. Because of the frequent awakening episodes, the total amount of sleep in elderly people is reduced and the pattern of their sleep is characterized by a relatively small amount, or even absence of Stage 4 (fig. 37). This decline of the "ability" to enter Stage 4 sleep is the cause of the fatigue feeling and sleepiness. As a result, elderly people have poor sleep and day naps are typical for them.

The light sleep of older people can be more easily disturbed than the deep sleep of the young. Therefore, the conditions which seem to insure a "good" sleep for a young worker are not necessarily satisfactory for elderly people.

Regardless of the differences in sleep patterns as related to age, there are other factors that may

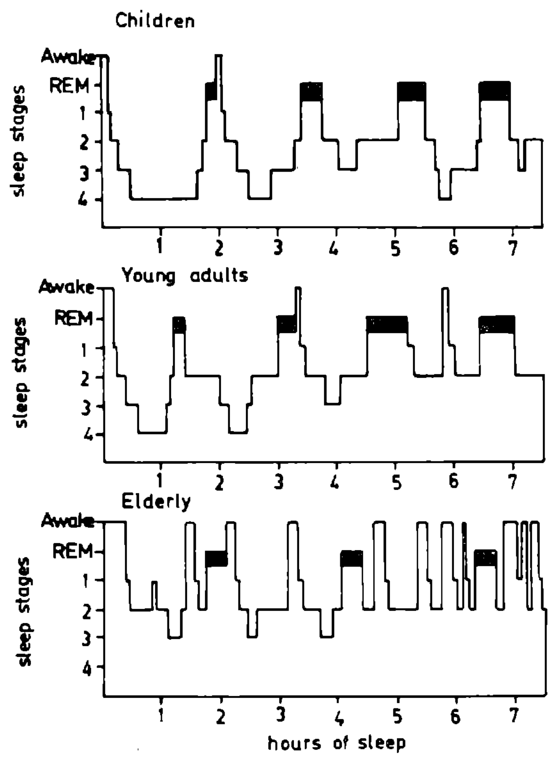


Figure 36. Sleep cycles of normal subjects. The sleep of children and young adults shows early preponderance of Stages 3 and 4, progressive lengthening of the first three REM periods, and infrequent awakenings. In elderly adults, there is little or no Stage 4 sleep, REM periods are fairly uniform in length, and awakenings are frequent and often lengthy (Kales, 1968).

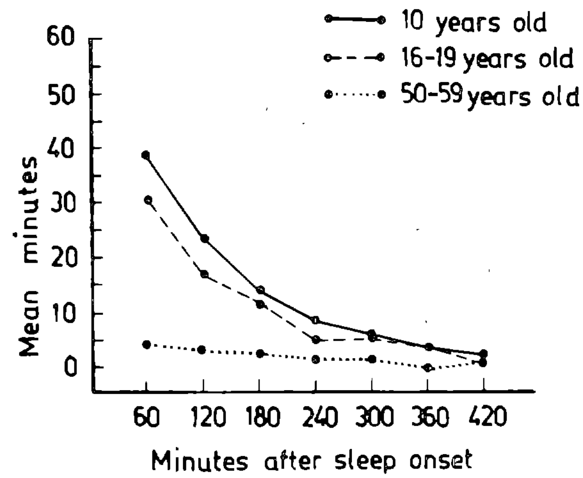


Figure 37. Amount of Stage 4 sleep during successive hours of night sleep in three groups of people (Webb, 1972).

change the sleep patterns. An essential role affecting sleep is the time of day during which one habitually sleeps or, rather, to a change in that habit. Generally, one falls asleep without difficulties if the time for going to sleep is consistent. However, during the period of the night shift the sleep-wake cycle is inverted. Changing the sleep hours leads to qualitative, as well as, quantitative changes in sleep pattern (3,143,179,266, 268,271,272). These changes occur under artificial conditions with the subjects removed from environmental influences. First of all, the waking episodes appear more frequently in the daytime than during the normal night sleep. Accordingly, there is a reduction in the amount of actual sleep in the daytime even in situations when the length of time devoted to sleep is the same as at night (fig. 38). Also, the total amount of deep sleep during the daytime (Stages 3 and 4) is reduced with Stages 3 and 4 becoming shorter and less frequent. By contrast, the percentage of Stage 1 sleep is greater during day sleep than at night. Changes in the distribution of REM sleep is also seen.

From the above, one can conclude that day sleep is less effective than normal night sleep. Even under favorable circumstances, with possibilities of a sufficiently long day-rest period, the total length of sleep (especially deep sleep) is shorter for day than for night sleep. Therefore, it is highly important to organize free time after night duty to insure a satisfactory length of day sleep. As a matter of fact, only time for adequate sleep can compensate for the lack of sleep.

Many workers divide their day sleep after night duty into two parts. They fall asleep as soon as

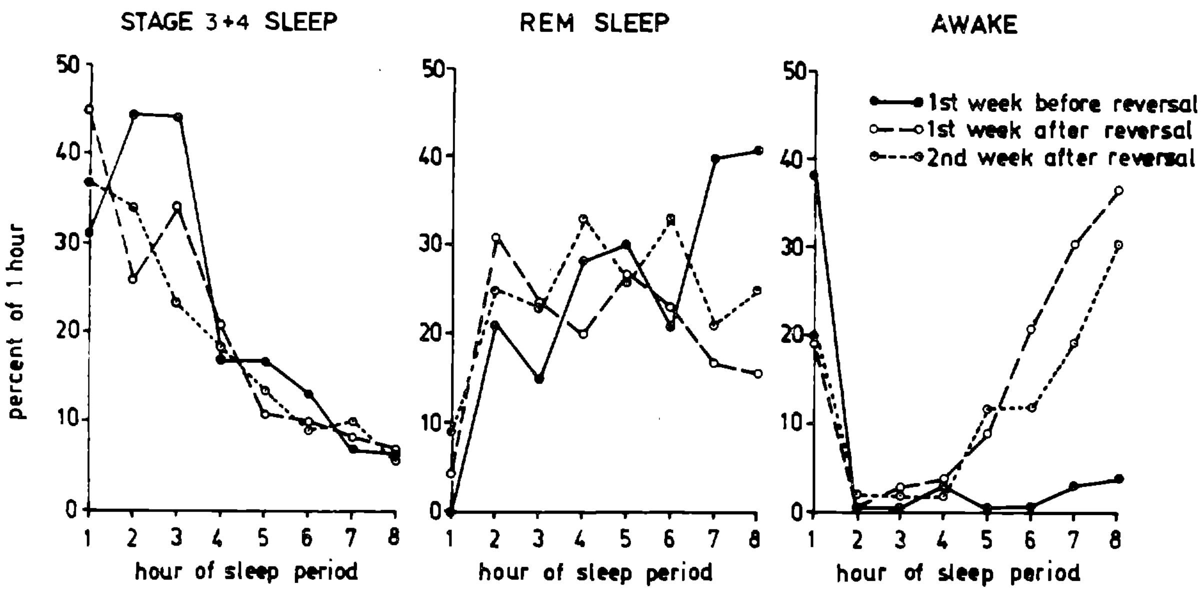


Figure 38. Mean percentage of sleep stages and the time of awakening for each hour of sleep period before and after reversal of the sleep-wake cycle. The subjects (five healthy young men, who normally slept at night in their prestudy activities) slept for 1 week at night between 10 p.m. to 6 a.m., then (after reversal) for 2 weeks during the day between 10 a.m. to 6 p.m. (Weitzman et al., 1970).

possible after coming home, and then they have a nap after dinner, before going to work. Some workers claim that the additional afternoon sleep is indispensable for them to maintain their efficiency at a relatively high level during night duty. They report being "particularly sleepy and tired on night shifts because of the lack of a preceding afternoon nap." However, workers who live far from their work can rarely afford the time to nap in the afternoon. Also, non-occupational activities and difficulties connected with public transport* can render the afternoon sleep impossible. In reality, a long time spent traveling to work and returning home means a reduction in sleep time, primarily the lack of an afternoon nap.

The role of afternoon sleep in maintaining a relatively high efficiency during night work has been confirmed in recent studies of pilots performed by Boesler and Ignatiuk (31). The authors controlled the performance of pilots during simulated night flights. These pilots (12 subjects) were studied during duty at night after they spent the afternoon in active rest (walking, visiting the museum, experiment A, and after sleeping for three hours in the afternoon, experiment B). To allow for the possible effects of training, the subjects were divided into two groups (six subjects each) with one group starting with experiment A, and the other with experiment B. It was shown that the number of deviations from pre-set range, speed, and altitude, as well as, the number of errors which constitute flight-risks, increased when the subjects were awake throughout the afternoon before night duty (experiment A). The conclusion was that active rest is not an acceptable substitute for sleep.

The significant role of afternoon sleep in the performance of night work seems to have been clarified somewhat by the studies of Karacan, et al. (130). Their electroencephalographic analysis of the sleep pattern of healthy young men (students) demonstrated a decrease in the total Stage 4 sleep of normal night sleep after the men had taken daytime naps. This leads to the suggestion that the afternoon nap causes a lowering of the "requirement" for sleep during the night. It also seems to support a common belief that one should take a nap in the afternoon before going to night work and should avoid an afternoon nap if a good night's sleep is desired.

Complaints of fatigue and sleepiness are common among shift workers, especially when they work on night shift. Usually, the night shift deficit

---

* Problems arising from the unsatisfactory quality of public transport have been described by some authors (201,205). From these data it follows that some workers are spending 2 to 3 hours daily commuting. According to Quaas (207, 208) the time spent for reaching work and going back home may increase during the period of afternoon and night shifts by 10 and 20 percent relative to morning shift, respectively.

of sleep can be compensated for only after a few days on the day shift. However, chronic sleep deprivation can affect the worker. There are numerous studies on the effects of sleep deprivation upon health, the various functions of the body, and mental and psychomotor performance (27,35,72,80,83,85,126,155,165,191,196,200,252,253,273,274,275). Elevation of plasma cholesterol, decrease of fibrinolysis, changes in ECG and EEG, and changes in body temperature are described. Changes in the structure of cells of the central nervous system are noted in experimental animals. Many authors described significant changes in the pattern of sleep during recovery from sleep deprivation (2,25,61,143,173,202,216,265). The changes, observed for several consecutive nights, consist mainly of an increase of the total amount of Stage 4 sleep. According to Sampson (224), prominence of the NREM sleep after sleep deprivation supports its particular role in removal of fatigue.

According to Bannel and Dervillee (18), the irregular life routine of shift workers and their chronic lack of sufficient sleep can lead to premature aging. The deficit of sleep (together with irregular meals, closely connected with shift work) can cause a deterioration of health during the course of some diseases. Caution is expressed against the employment for shift work of subjects with diabetes, hyperthyrosis, and gastrointestinal, cardiovascular, or nervous disorders. It seems also indisputable that epilepsy should be taken as a strong contraindication for assignment to night work, because a sleep deficit may provoke an epileptic attack. There is evidence that the onset of the first convulsion in a once apparently healthy subject can be casually connected with sleep deprivation (26,66,67,230).

CHAPTER VI

SOCIAL PROBLEMS OF SHIFT WORKERS AND ORGANIZATION OF NIGHT SHIFT

"For a majority of the people, night work means . . . something at variance with human nature, a deviation from its basic laws, a forced compromise with living conditions of our civilization . . . "

— *H. Valentin*

REASONS FOR PREFERENCE OF VARIOUS WORK SHIFTS

Reasons that workers give for preferring a given shift and shift system are rarely only specifically job related. The most important and decisive considerations are social, financial, and domestic (53,60,74,102,240,244,245,269). A majority of workers prefer the morning shift because it does not disturb the schedule of family and social life, does not restrain attendance at cultural and sports events, but does permit rest at night (102,103,104,201,241,243). The least preferred is the night shift with the afternoon shift also unpopular among most workers. The night and afternoon shifts dislocate normal home life.

Each shift may be characterized by a peculiar set of social difficulties (190): the afternoon worker is limited in his duty as a father; the night worker as a husband. Afternoon shifts take away the chance of spending time with the family and to unmarried people, it means a serious obstacle in their social relationships with friends. It also interfered with relaxation and active rest from participation in sports activities. On the other hand, from interviews with workers with marital conflicts, it appears that some of them prefer shift work because it provides an excuse to spend afternoons and nights away from home. A few people, who like solitary activities such as gardening, fishing, motoring, and woodworking, sometimes prefer night shifts and devote the daytime to their hobbies which otherwise would be neglected.

For many workers and their families, the most compelling reason for undertaking night or shift work is financial considerations. In spite of all the negative aspects of shift work, the shift system is often preferred by many workers because it is better paid.

VARIOUS TYPES OF SHIFT SYSTEMS

For a long time the apparent lack of adaptation to night work was attributed to the short period of a week on the night shift in the system of rotation. However, the extension of working nights beyond a week did not improve the situation, but instead, resulted in diminished work and efficiency, and increased absenteeism in the second week of night work (53,256,287). Periods on the night shift of more than a week were also poorly received by the workers themselves, mainly because participation in community and family life and contacts with people working on the day shifts became practically impossible. Thus, according to Eustace (74), assignment to a night shift for periods lasting a fortnight or even a month should be introduced only when it does not create excessive social difficulties and under conditions which enable workers to sleep undisturbed during the daytime.

There are many variations of the shift system:

some systems are traditional in a given part of a country; some are typical for a particular type of industry; and some arise from production requirements (189,229). Generally, in industries with a continuous 5-day per week operation, various types of three team-three shift systems are most common; for industries with full week continuous operation a four or five team three or four shift system is usually chosen.

In the traditional three shift system, work starts at about 6 a.m., 2 p.m., and 10 p.m. on the morning, afternoon, and night shifts, respectively. In a four shift work system (with 6-hours duty), there are two night shifts, the evening (6 p.m. to midnight) and the proper night shift (midnight to 6 a.m.). The advantage of this system is that the worker can spend at least part of the night asleep. Utilizing this principle, Eustace (74) proposed modifying the three shift system in such a way that the two shifts would each take only part of the night, leaving the rest for sleep. The suggested schedule would be: 1 a.m. to 9 a.m.; 9 a.m. to 5 p.m.; and 5 p.m. to 1 a.m. Such a shift schedule would not disturb the normal circadian sleep-wake cycle as much as the usual three shift rotation.

Eranko (71) proposed to replace the normal 24-hour day with a 25-hour "day" for shift workers. This 25-hour period would be subdivided into a work period lasting 8 hours and 20 minutes and an off-time period lasting 16 hours and 40 minutes. Thus, on each succeeding day, the shift would start and end an hour later (i.e., it would last from 8 a.m. to 4:20 p.m., then 9 a.m. to 5:20 p.m., and so on). The author expected that the slowly progressing change of the day work hours into night work hours would bring about a gradual adaptation to night work. An attempt to introduce a similar system was made by Wedderburn (270). He studied the sleep pattern in a "25-hour day" in groups of shift workers. However, the author noticed that the new system was not attractive, especially to the married men. Avoiding the interference with family life was sometimes more important to the workers than the sleep itself. In fact, several people preferred fixed hours of work, even in the case of night work, because then they could more easily adjust their sleep hours to the life schedule of the family (62).

From the physiological point of view, distribution of the off-time periods throughout the shifts is important. Combining a few days off with a long period of continuous shift work is not desirable and usually is not acceptable to the workers themselves, regardless of the fact that such a system would offer better possibilities for more convenient and attractive arrangement of holidays. For instance, in some systems with a six-day rotation, a three-days off-period is given after 18 days of shift work (21,22,42). According to the opinion of workers, however, the three days off was too short for recovery after such long, uninterrupted work.

In general, the frequency of complaints related to fatigue and sleepiness are greater among shift workers than among only day workers. Dirken (63), who recorded the complaints of shift and non-shift workers by means of a standardized questionnaire, noticed that the most frequent complaint of shift workers was that they come "home from work and fall asleep in a chair." Similarly, a tendency to take more and longer naps outside the major sleep period was observed by Tune (253) in shift workers compared to non-shift working control subjects.

Cameron (40) noted the frequency among shift and night workers of symptoms typical of fatigue, such as general irritability, restlessness and disturbance of sleep: "It (fatigue) has its origins in the personal state of the individual, and the appropriate starting point for research on fatigue is a volume of complaint from those who are exposed to a particular set of conditions. . . . It is necessary to examine the whole life pattern of those who are complaining of fatigue. Particular importance attaches to sleep habits, since fatigue effects bear a close resemblance to the effects of sleep deprivation. . . . The importance of such long term effects suggests that the time required for recovery may be a useful method of quantifying severity of fatigue." It is worth considering whether the method proposed by the author for evaluating fatigue (based on the length of time required for the recovery) could be useful in estimating tolerance to night work and to a shift system.

In the weekly rotation of shifts (with free Sunday), the afternoon shift to the night shift sequence rather than the night shift to the morning shift is often preferred because of the longer off-time period after the night shift (23,90,223). However, workers often contend that a schedule on the night shift for 1 week is too exhausting and that free Sundays and 2 weeks on the day shift are not sufficient to recover from the loss of sleep. Most investigators report that fatigue from night work is most annoying at the end of the week (88,89,99,201,283,284,290). This seems to be an argument against the concept that adaptation to night work could be achieved under shift work circumstances. In this context, a different opinion was recorded from a group of workers by Froberg, Karlsson, and Levi (84). These authors found that fatigue ratings were lower towards the end of the week as compared with the beginning.

According to Knauth and Rutenfranz (143) at least 24 hours are needed to make up for the sleep deficit resulting from spending one full night at work. Actually, there is a general tendency to prefer the system based on a rapid shift rotation, limiting the period of night shift to two or three consecutive nights. The idea of rapid rotation is supported by many authors (5,17,21,33,87,91, 144,174,253,261,269), and it has been introduced into several factories with remarkable success where economy and health are concerned. When work output and absenteeism were compared for groups of workers employed on six (or seven) and two (or three) days rotation systems, the latter appeared better. Such a system is also usually preferred by the workers (Table 6). Interviews indicated that the workers felt less fatigue, and had more time at their disposal for sleep, as well as, for family and social life. As a rule, the workers opposed to return to the traditional shift system with weekly rotation. Thus, the idea of physiological adaption to night work should be abandoned since such adaption is not encountered in most life situations.

Some objections against the general introduction of rapid shift rotation seem to result from a reluctance to change traditional habits of weekly rotations and from a fear of social consequences. In many families with both husband and wife working on a shift system, both of them have to coordinate their shift work in light of the care needs of their children.

The rapid shift system may be easily organized when four teams (or even more) participate in the system. However, complications arise when the rapid shift system is organized for only three teams of workers. The schedule of such a three-team system designed for the cotton industry by the Institute of Occupational Medicine in Lodz is presented in figure 39 (273). Advantages of this pattern are as follows: (1) the night shift occupies only two consecutive nights, (2) the period of night shift is always followed by 24 to 48 hour off-time, (3) the off-time period (including Sunday) always lasts 48 hours, and (4) apart from the free Sunday, there is a 24 hour off-time in the middle of every week. Such a system would assure better rest and recuperation than a weekly rotation.

TABLE 6

	Subject	Meal Arrangements	Sleep Arrangements	Work	Health	Social Life	Wife's Preferences
Chemical works (50 persons)	3x2x2 preferred	9	25	31	28	37	30
	About the same	34	19	10	17	5	2
	7-day shift preferred	5	5	5	3	7	7
	(Don't know Not applicable Not asked)	2	1	4	2	1	11
Steel works (60 persons)	2x2x2 preferred	25	39	43	26	48	41
	About the same	26	14	14	29	7	1
	7-day shift preferred	6	5	0	0	4	1
	(Don't know Not applicable Not asked)	3	2	3	5	1	17

Table 6. Numbers of men who preferred the new and the former (7-shift-cycle) systems with respect to the subjects listed, three years after introducing the new system (Walker, 1966).

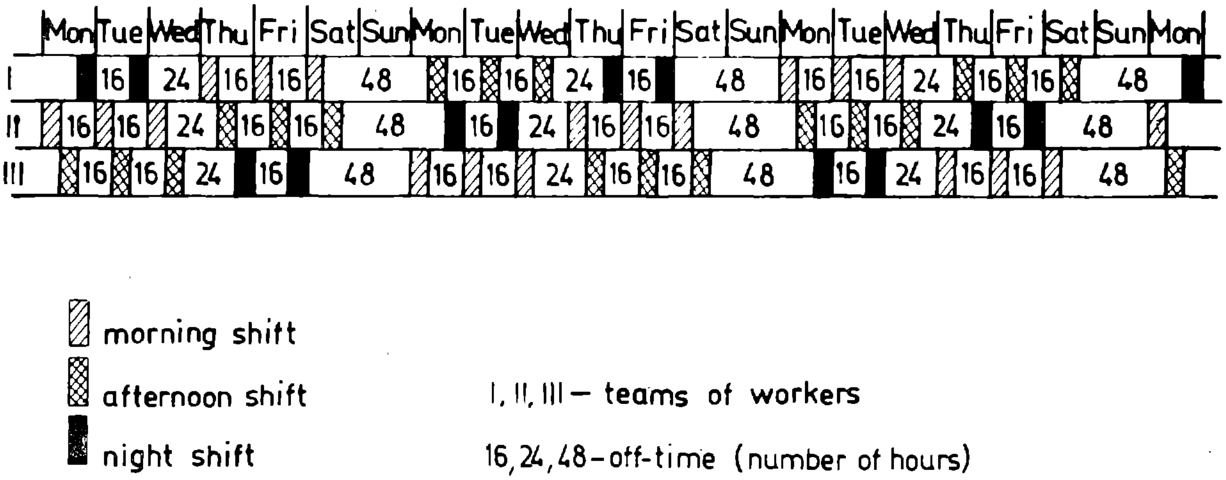


Figure 39. Scheme of rapid shift system proposed by the Institute of Occupational Medicine in Lodz for three teams of workers employed in a cotton industry. The total work time amounts, on the average, to 42.7 hours per week (Wojtczak-Jaroszowa, 1973).

ORGANIZATION OF BREAKS WITHIN THE NIGHT SHIFT

There is insufficient literature on the need for breaks during the night shift. Most often, the emphasis is on limiting total effective working time at night to correspond with that of day shifts (17,21,205,236). Shortening the total working time of the night shift by more frequent, or longer break periods is recommended. This is especially important in exhausting physical work, or in monotonous or vigilance situations. Greater fatigue in night shift workers was indicated by prolonged breaks occurring more often during night shifts than during the day (Quaas, 207). Also, the data presented in all preceding chapters support establishing different patterns of work and breaks within all three shifts.

A subjective feeling of drowsiness and fatigue during the night shift is usually strongest between 2 a.m. and 5 a.m. Some workers fall asleep for short periods at work, claiming that otherwise, they would not be able to continue work. Hakkinen (102) interviewed shift workers who, every hour, assessed their subjective feeling of fatigue and sleepiness. According to his observations (fig. 40a), complaints of fatigue occurred at the beginning of the morning shift and toward the end of the afternoon shift. However, most complaints were noted on the night shift at about 4 a.m. The curve of fatigue is similar to the curve of spinners' decreased efficiency described by us (fig. 40b). The curve of errors in studies by Bjerner and Swensson (fig. 40c) was similar to the curve of changes in delay in answering calls by teleprinter switchboard operators reported by Browne (fig. 40d). The similarity among those curves and, also, to the diurnal changes in numerous physiological functions, is remarkable.

The similarity of curves suggests that the use of longer rest breaks during the night shift would be appropriate at the time when the drowsiness is most annoying and work efficiency declines. Similar suggestions have been put forward by other authors even though the opinions on how to use the breaks are different. Some observers (22,88,89) suggest that active exercise should be introduced during the break at night to combat sleepiness. On the contrary, Babadzhanyan and Muksinova (17) claim that the ability for further work can be restored if the workers are allowed to sleep during the break. They recommended using a 1-hour break between 2 a.m. and 3 a.m. for sleep. A similar solution has been introduced in Japan (254) where in the majority of industries, a 1-hour period for sleep between 1 a.m. and 4 a.m. was introduced for night shift workers.

Meal schedules pose a separate and important point in the organization of night shift work. A majority of workers are not accustomed to eating during the night shift and usually limit their intake to only fluids (21,23,102,181,203). This results from a lack of appetite during the night shift despite muscular activity. Loss of body weight in shift workers is, therefore, often observed after a prolonged period of night work.

Takagi (240), discussing the physiological mechanisms of hunger, assumed that due to the predominance of the parasympathetic nervous system, meals should be consumed willingly at night. In reality, however, the opposite is true. Eating during the night is usually not observed even in workers on the shift system for a long time (181,203,283,284). Sometimes a worker will eat his meals when he first starts on a night shift schedule, but by the end of the week, he takes his food back home (203).

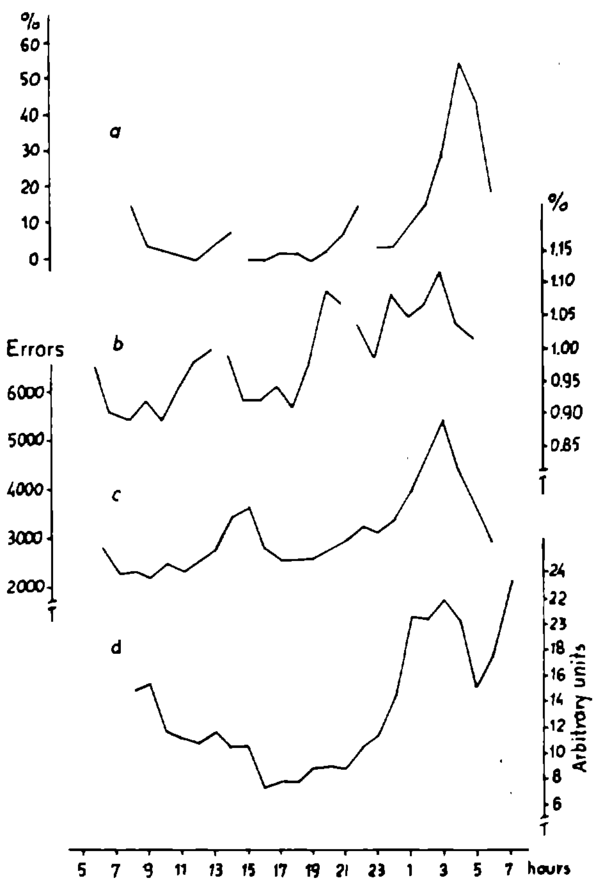


Figure 40. Feeling of fatigue (a. Hakkinen, 1966) and work efficiency of shift workers during their work on different shifts (b. Wojtczak-Jaroszowa and Pawlowska-Skyba, 1967; c. Bjerner and Swensson, 1953; and d. Browne, 1949).

Hakkinen (102) reported (fig. 41) that the feeling of hunger was strongest at about noon and at 6 p.m. on the morning and afternoon shift, respectively. These hours correspond to normal meal times, although, the results could be somewhat different in other populations, with different meal habits. However, hunger was at its minimum during the night shifts. At about 3 a.m., i.e., after four hours of work when food should be consumed, the workers expressed no desire for food.

The irregularity of the daily meals of shift workers has attracted the attention of numerous investigators (1,37,74,121,178,244,247,248, 286). This irregularity, connected with shift work, disrupts therapy for numerous disorders (e.g., diabetes and gastro-intestinal disorders) where regular daily meals form a basis of treatment. Therefore, some diseases may be aggravated by shift work, and in these cases, the workers should not be put on the night shift. Irregular nourishment is also taken into consideration as a factor in the development of peptic ulcers. Very often, the

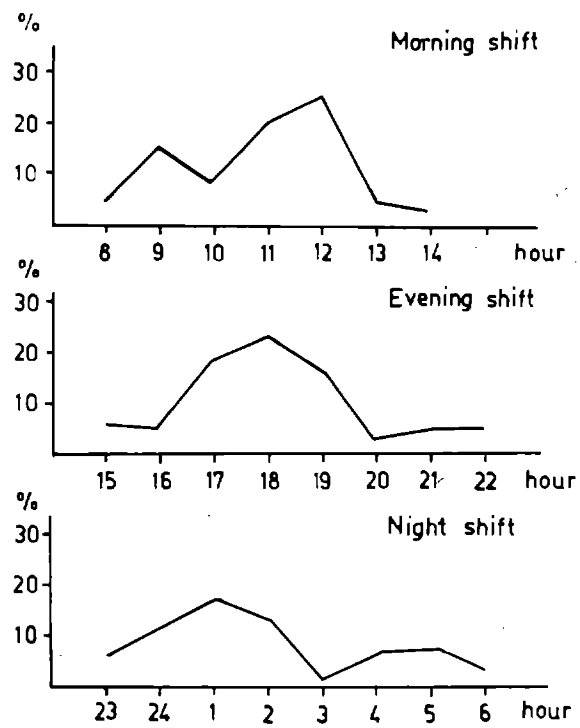


Figure 41. Distribution of complaints about the feeling of hunger in relation to working hours during different shifts (Hakkinen, 1966).

transfer of a worker from shift work to the regular day shift is indispensable for the treatment of peptic ulcers. The number of shift workers with gastro-intestinal disorders is higher among young men than among older workers.

Although beyond the scope of this discussion, it should be mentioned that the working hours of shift workers often determines not only the worker's own meal pattern, but also meal times of the families (222). This applies especially to when the meal schedule may be adjusted to the hours of the shift worker's day sleep.

REFERENCES

1. Aanonsen, A. (1963): *Shift Work and Health.* Norwegian Monographs on Medical Science. Universitetsforlaget, Oslo.
2. Agnew, H.W., W.B. Webb, and R.L. Williams (1964): *The effects of stage four sleep deprivation.* **Electroenceph. Clin. Neurophysiol.** 17:68.
3. Agnew, H.W., W.B. Webb, and R.L. Williams (1968): *Sleep cycle reversal.* **Psychophysiology** 5:216.
4. Airaksinen, M.M., and H. Karppanen (1970): *Effect of pinealectomy and oxypertine on hypothalamic FSH-releasing factor and circadian activity rhythm in rats.* **Scand. J. Clin. Lab. Invest.** 25 (Suppl. 113):43.
5. Andlauer, P., and L. Fourre (1963): *Effects physiologiques et physiopathologiques de la periodicite de rotation dans le travail en equipes alternantes.* XIV Int. Congr. Occup. Health, Madrid, 1309.
6. Armstrong, R.H., D. Burnab, A. Jacobson, A. Kales, S. Ward, and J. Golden (1965): *Dreams and gastric secretion in duodenal ulcer patients.* **New Physician** 14:241.
7. Aschoff, J. (1955a): *Exogene und endogene Componente der 24-Stunden-Periodik bei Tier und Mensch.* **Naturwissenschaften** 42:569.
8. Aschoff, J. (1955b): *Der Tagosgang der Korpertemperatur beim Menschen.* **Klin. Wochschr.** 33:545.
9. Aschoff, J. (1958): *Timegivers of 24-hour physiological cycles. In: Man's Dependance on the Earthly Atmosphere,* K. E. Schaefer, Ed. Macmillan Company, New York.
10. Aschoff, J. (1965): *Circadian rhythms in man.* **Science** 148:1427.
11. Aschoff, J. (1969): *Desynchronization and resynchronization of human circadian rhythms.* **Aerospace Medicine** 40:844.
12. Aschoff, J. (1970): *Circadiane Periodik als Grundlage des Schlaf-Wach-Rhythmus.* In: *Ermudung, Schlaf und Traum,* W. Baust, Ed. Stuttgart.
13. Aschoff, J., H. Giedke, E. Poppel, and R. Wever (1972): *The influence of sleep interruption and of sleep deprivation on circadian rhythms in human performance.* In: *Aspects of Human Efficiency,* W.P. Colquhoun, Ed., English Universities Press Ltd., London.
14. Aschoff, J., and A. Heise (1972): *Thermal conductance in man: its dependance on time of day and on ambient temperature.* In: *Advances in Climatic Physiology,* S. Itoh, Ed. Igaku Shoin Ltd., Tokyo.
15. Astrand, P.O., and I. Ryhming (1954): *A nomogram for calculation of aerobic capacity physical fitness from pulse rate during submaximal work.* **J. Appl. Physiol.** 7:218.
16. Astrand, P.O., and K. Rodahl (1970): *Textbook of Work Physiology.* McGraw Hill, New York.
17. Babadzhenyan, M.G., and L.A. Muksinova (1966): *O sutochnoi periodike fiziologicheskikh funkeii organizma cheloveka i racionalnom regulovanii nochnogo truda.* **Gig. Truda** 10:9:3.
18. Bannel, F., and E. Dervillee (1969): *Le travail de nuit apercus socio-professionnels et medicaux.* XVI Int. Congr. Occup. Health, Tokyo, 107.
19. Baranski, S., K. Kwarecki, and S. Szmigielski (1972): *Contemporary problems of chronobiology.* (Polish) **Post. Hig. i Med. Dosw.** 26:291.
20. Bardswell, N.D., and J.E. Chapman (1911): *Some observations upon the deep temperature of the human body at rest and after muscular exertion* **Brit. Med. J.** 11:1106.
21. Barhad, B., and M. Pafnote (1969): *Contributions a l'etude du travail on equipes alternantes.* Proc. Int. Symposium on Night and Shift Work, Oslo, 84.

22. Barhad, B., and M. Pafnote (1970): *Contributions a l'etude du travail en equipes alternantes.* **Le Travail Human** 33:1.
23. Bartolozzi, O. (1962): *Lavoro notturno e turni di lavoro.* **Med. Lavoro** 53:198.
24. Bartter, F. C., C. S. Delea, and F. Halberg (1962): *A map of blood and urinary changes related to circadian variations in adrenal corticol function in normal subjects.* **Ann. N.Y. Acad. Sci.** 98:969.
25. Berger, R.J., and I. Oswald (1962): *Effects of sleep deprivation on behavior, subsequent sleep, and dreaming.* **J. Ment. Sci.** 108:457.
26. Bergonzi, P., C. Chiurulla, and E. Tempesta (1972): *Selective deprivation of sleep stages in epileptics.* In: *Sleep,* W.P. Koella, Ed. Basel, 534.
27. Bjerner, B. (1949): *Alpha depression and lowered pulse rate during delayed actions in a serial reaction test: A study in sleep deprivation.* **Acta Physiol. Scand.** 19 (Suppl. 65).
28. Bjerner, B., A. Holm, and A. Swensson (1955): *Diurnal variation in mental performance: A study of 3-shift workers.* **Brit. J. Industr. Med.** 12:103.
29. Bjerner, B., and A. Swensson (1953): *Schichtarbeit und Rhythmus.* **Acta Med. Scand. Suppl.** 278:102.
30. Bloch, M. (1964): *Rhythmic diurnal variation in limb blood flow in man.* **Nature** 202:398.
31. Boesler, P., and J. Ignatiuk (1972): *Negative influence of lack of afternoon nap on performance of pilots during flights at night.* (Polish) **Przeglad Psychologiczny** 15,4,2.
32. Bouhuys, A., F. Hartogensis, and H.J.H. Korfage (1963): *Byssinosis prevalence and flax processing.* **Brit. J. Industr. Med.** 20:320.
33. Brnadt, A. (1969): *On the influence of various shift systems on the health of the workers.* XVI Int. Congr. Occup. Health, Tokyo, 106.
34. Browne, R.C. (1949): *The day and night performance of teleprinter switchboard operators.* **Occup. Psychol.** 23:121.
35. Buck, L., and C.B. Gibbs (1972): *Sleep loss and information processing.* In: *Aspects of Human Efficiency,* W.P. Colquhoun, Ed. English Universities Press Ltd., London, 47.
36. Buley, L.E. (1970): *Experience with a physiologically based formula for determining rest periods on long distance air travel.* **Aerospace Medicine** 41:680.
37. Burger, G.C.E., M.R. van Alphen de Voer, G.A.T. Wesseldijk, M.H.K. von de Graaf, and A. Doornsbosch (1957): *Human problems in shift work.* XII Int. Congr. Occup. Health, Helsinki, 3:126.
38. Bunning, E. (1963): *Die Physiologische.* Springer-Verlag, Berlin.
39. Cade, R., D.L. Shires, M.V. Barrow, and W.C. Thomas (1967): *Abnormal diurnal variations of plasma cortisol in patients with renovascular hypertension.* **J. Clin. Endocr. Met.** 27:800.
40. Cameron, C. (1973): *A theory of fatigue.* **Ergonomics** 16:633.
41. Carrozzini, B., and A.B. Degli (1963): *Sui bioritmi della eliminazione urinaria dei 17-KS e degli 11-OS. Nei soggetti alternanti il lavoro diurno con turni di lavoro notturno.* **Arcisped. S. Anna Ferrara** 16:1131.
42. Carstocea, L., R. Elias, R . Mateescu, M. Cristescu, and G. Voicu (1966):*Some peculiarities of fatigue in shift work in an automatised section.* XV Int. Congr. Med. Travail, Vienna, IV, 99.
43. Chemin, P. (1968): *Les rythmes biologiques en Medicine du travail aerien.* **Arch. Mal. Prof.** 29:735.
44. Cloudsley-Thompson, J.L. (1961): *Rhythmic Activity in Animal Physiology and Behavior.* In: *Theoretical and Experimental Biology,* vol. 1. Acad. Press, New York and London.
45. Colin, J., J. Timbal, C. Boutelier, Y. Houdas, and M. Siffre (1968): *Rhythm of the rectal temperature during a 6-month free-running experiment.* **J. Appl. Physiol.** 25:170.
46. Colquhoun, W.P. (1971): *Circadian variations in mental efficiency.* In: *Biological Rhythms and Human Performance.* W.P. Colquhoun, Ed. Acad. Press., London and New York.
47. Colquhoun, W.P., M.J.F. Blake, and R.S. Edwards (1968a): *Experimental studies of shift-work. I: A comparison of "rotating and stabilized" 4-hour shift system.* **Ergonomics** 11:437.
48. Colquhoun, W.P., M.F.J. Blake and R.S. Edwards (1968b): *Experimental studies of shift work. II: Stabilized 8-hour shift systems.* **Ergonomics** 11:527.
49. Colquhoun, W.P., M.J.F. Blake, and R.S. Edwards (1969): *Experimental studies of shift work. III: Stabilized 12-hour shift systems.* **Ergonomics** 12:865.

50. Colquhoun, W.P., M.J.F. Blake, and R.S. Edwards (1969): *Experimental studies of shift work.* Proc. Int. Symposium on Night and Shift Work, Oslo, 47.
51. Conroy, R.T.W.L. (1967): *Circadian rhythm of 11-hydroxycorticosteroids in night workers.* **J. Physiol.** 191:21.
52. Conroy, R.T.W.L., A.L. Elliott, and J.N. Mills (1970): *Circadian excretory rhythms in night workers.* **Brit. J. Industr. Med.** 27:356.
53. Conroy, R.T.W.L. and J.N. Mills (1969): *Circadian rhythms and shift working.* Proc. Int. Symposium on Night and Shift Work, Oslo, 42.
54. Conroy, R.T.W.L., and J.N. Mills (1970): *Human Circadian Rhythms.* J. and A. Churchill, London.
55. Cotes, J.E. (1965): *Lung Function, Assessment, and Application in Medicine.* Blackwell Scientific Publications, Oxford.
56. Crane, J.E. (1963): *The time zone fatigue syndrome.* **Flying Physician** 7:19.
57. D' Agata, R. and R. Vigneri (1971): *Circadian variations of human growth hormone serum levels.* **Ann. d' Endocrin.** 32:384.
58. Daleva, M., I. Hadijilova, N. Tsaneva, and G. Raidovski (1971): *Physiological changes in operators during shift work.* Proc. of the Second Int. Symposium on Night and Shift Work, Slanchev Bryag 26.
59. Davey, C.P. (1973): *Physical exertion and mental performance.* **Ergonomics** 16:595.
60. De la Mare, G., and J. Walker (1968): *Factor influencing the choice of shift rotation.* **Occup. Psychology** 42:1.
61. Dement, W.C., and S. Greenberg (1966): *Changes in total amount of Stage IV sleep as a function of partial sleep deprivation.* **Electroenceph. Clin. Neurophysiol.** 20:523.
62. Dervillee, P., and Lazari (1957): *Reflexions on work by rotations and its effects on health.* Helsinki, 35.
63. Dirken, J.M. (1966): *Industrial shift work: Decrease in well-being and specific effects.* **Ergonomics** 9:115.
64. Doe, R.P., E.B. Flink, and M.G. Goodsell (1956): *Relationship of diurnal variation in 17-hydroxycorticosteroid levels in blood and urine to eosinophils and electrolyte excretion.* **J. Clin. Endocrin. Met.** 16:192.
65. Doe, R.P., J.A. Vennes, and E.B. Flink (1960): *Diurnal variations of 17-hydroxycorticosteroids, sodium, potassium, magnesium and creatinine in normal subjects and cases of treated adrenal insufficiency and Cushing's syndrom.* **J. Clin. Endocrin. Met.** 20:253.
66. Domzal, T., M. Holyst, A. Foss, and S. Zalejski (1970): *Electroencephalographical, biochemical, and psychological studies on the influence of lack of sleep upon nervous system of soldiers.* (Polish) **Lek. Wojskowa** 46:325.
67. Domzal, T., M. Holyst, A. Foss, and S. Zalejski (1972): *Sleep deprivation in healthy subjects and epileptics.* In: *Sleep,* W.P. Koella, Ed. Basel, 521.
68. Ehret, C.F., and E. Trucco (1967): *Molecular models for the circadian clock. I. The chronon concept.* **J. Theor. Biol.** 15:240.
69. Von Eiff, A.W. (1955): *Das Verhalten mehrerer Korperfunktionen wahrend eines 7 tagigen Rhythmus-Versuches und die Bedeutung des Zeitbewusstseins.* **Acta Med. Scand.,** Suppl. 307, 140.
70. Elmadjian, F., E.T. Lamson and R. Neri (1956): *Excretion of adrenaline and noradrenaline in human subjects.* **J. Clin. Endocrin. and Metab.** 16:222.
71. Eranko, O. (1957): *25-hour day: one solution to the shift work problem.* XII Int. Congr. Occup. Health, Helsinki, 37.
72. Evans, J.I., G.A. Christie, S.A. Lewis, J. Daly, and M. Moore-Robinson (1972): Sleep and time zone changes. A study in acute sleep reversal. **Archiv. of Neurol.** 26:36.
73. von Euler, U.S., S. Hellner-Bjorkman, and I. Orwen (1955): *Diurnal variations in the excretion of free and conjugated: noradrenaline and adrenaline in urine from healthy subjects.* **Acta Physiol. Scand.** 33 (Suppl. 118): 10.
74. Eustace, J.F. (1965): *Shift work.* **Ind. Med. and Surg.** 34:857.
75. Feigin, R.D., A.S. Klainer, and W.R. Beisel (1967): *Circadian periodicity of blood-amino acids in adult men.* **Nature** 215: 512.

76. Ferrari, E., P.A. Bossolo, S. Pallivacini, and C. Cebrelli (1968): *Parasimpaticolisi farmacologica e bioritmo circadiano della corticosteroiduria nell obesita ginoide.* **Rass. Neur. Veg.** 22:126.
77. Fiorica, V., M.J. Burr and R.B.S. Moses (1968): *Contribution of activity to the circadian rhythm in excretion of Magnesium and Calcium.* **Aerospace Medicine** 39:714.
78. Fiske, V.M. (1964): *Observations on adrenal rhythmicity and associated phenomena in the rat.* **Ann. N. Y. Ac. Sci.** 117:231.
79. Fort, A., and J.N. Mills (1972): *Influence of sleep, lack of sleep, and circadian rhythm on short psychometric tests.* In: *Aspects of Human Efficiency,* W.P. Colquhoun, Ed. English Universities Press Ltd., London, 115.
80. Foss, A. (1970): *Psychological studies of 48-hours sleep deprivation in healthy subjects.* **Lek. Wojsk.** 8:714.
81. Freeman, G.L., and C.I. Hovland (1934): *Diurnal variations in performance and related physiological processes.* **Psychol. Bull.** 31:777.
82.. Froberg, J., C.G. Karlsson, L. Levi, L. Lidberg, and K. Seeman (1969): *Circadian rhythms in catecholamine excretion, psychomotor performance and ratings of stress and fatigue during a 75-hour vigilance.* Proc. Int. Symposium on Night and Shift Work, Oslo, 64.
83. Frobèrg, J., C.G. Karlsson, L. Levi, and L. Lidberg (1970): *Circadian variations in performance, psychological ratings, catecholamine excretion and urine flow during prolonged sleep deprivation.* In: *Aspects of Human Efficiency; Diurnal Rhythm; and Loss of Sleep,* W.P. Colquhoun, Ed. English Universities Press Ltd., London.
84. Froberg, J., C.G. Karlsson, and L. Levi (1971): *Shift work: A study of catecholamine excretion, self-ratings, and attitudes.* Proc. Second Int. Symposium on Night and Shift Work, Slanchev Bryag, 10.
85. Froberg, J., C.G. Karlsson, L. Levi, and L. Lidberg (1971): *Physiological and biochemical stress reactions induced by psychosocial stimuli.* In: *Society, Stress, and Disease,* L. Levi, Ed. Oxford Univ. Press, London, 1:280.
86. Gagliardino, J.J., M.T. Pessacq, and O.R. Rebolledo (1971): *Circadian control of carbohydrate and protein metabolism in muscle.* Proc. IX, XXV Int. Congr., Munich, 193.
87. Gambashidze, G.M. (1961): *O znachenii sutochnoi periodichnosti fizjologicheskikh funkeii v ocenke rabotosposobnosti pri trekhsmennykh rabotakh.* **Gig. Truda** 6:13.
88. Gambashidze, G.M. (1964): *O znachenii sutochnogo ritma fizjologicheskikh funkeii dla ocenki rabotosposobnosti pri smennykh i nochnykh rabotakh.* Moskva Dissert.
89. Gambashidze, G.M. (1965): *O voznozhnosti prisposobleniia organizma k smennym i nochnym rabotam.* **Gig. Truda** 9:1:12.
90. Gambashidze, G.M. (1969): *Osobennosti fizjologicheskikh sdvigov pri monotonnom kharaktere truda v usloviiakh trekhsmennogo grafika.* **Gig. Truda** 13:8:13.
91. Gawrilescu, N., M. Pafnote, J. Vaida, L. Mihaila, L. Carstocea, O. Luchian and P. Poposco (1966): *Controlboard shift work turning every two days.* XV Congr. Int. Med. Travail v. IV, Vienna, 103.
92. Gerritzen, F. (1955): *Der Stoffwechselstrom.* **Acta Med. Scand.,** Suppl. 307:150.
93. Gerritzen, F., T. Strengers, and S. Esser (1969): *Studies on the influence of fast transportation on the circadian excretion pattern of the kidney in humans.* **Aerospace Medicine** 40:264.
94. Geschicter, E.H., P.A. Andrews, and R.W. Bullard (1966): *Nocturnal body temperature regulation in man: a rationale for sweating in sleep.* **J. Appl. Physiol.** 21:623.
95.. Ghata, J., F. Halberg, A. Reinberg, and M. Siffre (1969): *Rythmes circadiens desynchronises du cycle social (17-hydroxycorticosteroides, temperature rectale, veille-sommeil) chez deux sujets adultes sains.* **Ann. d' Endocrin.,** Paris 30:245.
96. Gielec, L. (1973): *Circadian variations in pulmonary ventilation in men. (Polish)* **Med. Pracy** 34:415.
97. Gradina, C. (1963): *Recherches sur le rythme de travail journalier et hebdomadaire.* XIV Int. Congr. Occup. Health, Madrid, v. III, 1420.
98. Graf, O. (1934): *II Mitteilung,* **Arbeitsphysiologie** 7:334; *III Mitteilung,* **Arbeitsphysiologie** 7:359; *IV Mitteilung,* **Arbeitsphysiologie** 7:381.

99. Grandjean, E.P., and G. Wotzka (1969): *Fatigue related to day-time and night-time and to the duration of work hours in air traffic controllers.* XVI Int. Congr. Occup. Health, Tokyo, 100.
100. Grandjean, E.P., G. Wotzka, R. Schaad, and A. Gilgen (1971): *Fatigue and stress in air traffic controllers.* **Ergonomics** 14:159.
101. Guberan, E., M.K. Williams, J. Walford, and M. M. Smith (1969): *Circadian variation of F.E.V. in shift workers.* **Brit. J. Industr. Med.** 26:121.
102. Hakkinen, S. (1966): *Psychological and physiological reactions to shift work.* XV Congr. Int. de Medicine du Travail, Vienna, v. IV, 87.
103. Hakkinen, S. (1969): *Adaptability to shift work.* Proc. Int. Symposium on Night and Shift Work, Oslo, 68.
104. Hakkinen, S. and O. Kammonen (1971): *Adaptability to shift work.* Abstract of the Int. Conf. of the Permanent Commission and Int. Association of Occup. Health, Slanchev Bryag, 115.
105. Halasz, B., I. Vernikos-Danellis, and R.A. Gorski (1967): *Pituitary ACTH content in rats after partial or total interruption of neural afferents to the medial basal hypòthalamus.* **Endocrinology** 81:921.
106. Halbert, F. (1953): *Some physiological aspects of 24-hour periodicity.* **Lancet** 73:20.
107. Halberg, F. (1955): *Experimentelles zur Physiologie des Bebeunierenzyklus.* **Acta Med. Scand.**, Suppl. 307, 117.
108. Halberg, F. (1962): *Physiologic 24-hour rhythms a determinant of response to environmental agents.* In: **Man's Dependence of the Earthly Atmosphere,** W.K.E. Shaefer, Ed. MacMillan Company, New York, 43.
109. Halberg, F., A.F. Lyle, and R.J. Gully (1958): *24-hour rhythms in rectal temperature and blood eosinophils after cortication in human subjects.* **J. Appl. Physiol.** 12:381.
110. Hale, H.B., E.W. Williams, E.N. Smith, and C.E. Melton (1971): *Neuroendocrine and metabolic responses to intermittent night shift work.* **Aerospace Medicine** 42:156.
111. Hamilton, P., R.T. Wilkinson, and R.S. Edwards (1972): *A study of four days partial sleep deprivation.* In: **Aspects of Human Efficiency,** W.P. Colquhoun, Ed. English Universities Press, Ltd., London, 101.
112. Heikkinen, E., H. Karppanen, H. Vapaatalo, and O. Pelkonen (1973): *Lack of effect of pinealectomy on the diurnal rhythm in drug metabolism.* **Acta Pharmacol. et Toxicol.** 32:157.
113. Heiser, F., and L. Cohen (1953): *Diurnal variation of skin temperature.* **J. Industr. Hyg.,** v. XV, 243.
114. Hildebrandt, G. (1955): *Untersuchungen uber die rhythmische Funktionsordnung von Puls und Atem.* **Acta Med. Scand.** Suppl. 307, 175.
115. Hildebrandt, G., and P. Engel (1972): *The relation between diurnal variations in psychic and physical performance.* In: **Aspects of Human Efficiency,** W. P. Colquhoun, Ed. English Universities Press, Ltd., London, 231.
116. Hildebrandt, G., P. Engelbertz, and G. Hildebrandt-Evers (1954): *Physiologische Grundlagen fur eine tageszeitliche Ordnung der Schwitzprozeduren.* **Z. Klin. Med.**, 152:446.
117. Hill, L., and M.B. Lond (1898): *On rest, sleep, and work and concomitant changes in the circulation of the blood.* **Lancet** 1:282.
118. Hollwich, F., and B. Dieckhues (1971): *Endocrine system and blindness.* **Dtsch. Med. Wochenschr.** 96:363.
119. Holmgren, H.J., and A. Swensson (1953): *Der Einfluss des Lichtes auf den 24-Stunden-Rhythmus der Aktivitat, des Leberglykogens und der korpertemperatur.* **Acta Med. Scand.,** Suppl. 278, 71.
120. Hoyer, K. (1944): *Physiologic variations in the iron content of human blood serum. I. The variations from week to week, from day to day, and through twenty-four hours.* **Acta Med. Scand.** 119:562.
121. Ihre, B.J.E., and R. Muller (1943): *Gastric and duodenal ulcer.* **Acta Med. Scand.** 116:33.
122. Jansen, G., J. Rutenfranz, and R. Singer (1966): *Uber eine circadiane Rhythmik sensumotorischer Leistungen.* **Int. Z. Angew. Physioleinschl. Arbeitsphysiol.** 22:65.
123. Januszewicz, W., and B. Wocial (1960): *Influence of the work, circadian rhythm, and visual stimuli upon catecholamines urinary excretion.* (Polish) **Pol. Arch. Med. Wewn.** 30:207.
124. Johnson, L. (1972): *Invited Comment in General Discussion 75-77.* In: **Aspects of Human Efficiency,** W.P. Colquhoun, Ed. English Universities Press, Ltd., London.

125. Jori, A.D., E. Salle, and V. Santini (1971): *Daily rhythmic variation and liver drug metabolism in rats.* **Biochem. Pharmacol.** 20:2965.
126. Jovanovic, U.J. (1971): *Bioelectric and diurnal rhythmic changes following long experimental deprivation of sleep in man.* **Electroenceph. and Clin. Neurophysiol.** 30:167.
127. Kales, A. (1968): *Sleep and dreams: Recent research on clinical aspects.* **Ann. Intern. Med.** 68:1078.
128. Kaneko, M., F.W. Zechman, and R.E. Smith (1968): *Circadian variation in human peripheral blood flow levels and exercise responses.* **J. Appl. Physiol.** 25:109.
129. Kano, H. (1971): *Inspection task. Psychological aspects of inspection tasks.* **J. Sci. Lab.** 47:173.
130. Karacan, I., R.L. Williams, W.W. Finley, and C.J. Hursch (1970): *The effects of naps on nocturnal sleep: influence on the need for Stage 1-REM and Stage 4 sleep.* **Biol. Psychiatry** 2:391.
131. Kawakami, S., S. Yamaoka, and T. Yamaguchi (1972): *Influence of light and hormones upon circadian rhythm of EEG slow wave and paradoxical sleep.* In: *Advances in Climatic Physiology,* S. Itoch, K. Ogata, and H. Yoshimura, Ed. Igaku Shoin, Ltd., Tokyo, 349.
132. Klaus, E.J., and D. Clasing (1960): *Untersuchungen zur Tagesrhythmik der Pulswellengeschwindigkeit beim Sportler.* **Int. Z. Angew. Physiol.** 18:319.
133. Klein, K.E., H. Bruner, R. Finger, K. Schalkhauser and H.M. Wegmann (1966): *Tagesrhythmik und Funktiondiagnostik der peripheren Kreislaufregulation.* **Int. Z. Angew. Physiol.** 23:125.
134. Klein, K.E., H. Bruner, H. Holtmann, H. Rehme, J. Stolze, W.D. Steinhoff, and H.M. Wegmann (1970): *Circadian rhythm of pilots efficiency and effects of multiple time zone travel.* **Aerospace Medicine** 41:125.
135. Klein, K.E., H.M. Wegmann, and H. Bruner (1968): *Circadian rhythm in indices of human performance, physical fitness, and stress resistance.* **Aerospace Medicine** 39:512.
136. Klein, K.E., H. M. Wegmann, and B.J. Hunt (1972): *Desynchronization of body temperature and performance circadian rhythm as a result of outgoing and homegoing transmeridian flights.* **Aerospace Medicine** 43:119.
137. Kleitman, N. (1949): *Biological rhythms and cycles.* **Physiol. Rev.** 29:1.
138. Kleitman, N. (1963): *Sleep and Wakefulness.* Univer. of Chicago Press, Chicago.
139. Kleitman, N., D.P. Jackson (1950): *Body temperature and performance under different routines.* **J. Appl. Physiol.** 3:309.
140. Kleitman, N., and E. Kleitman (1953): *Effect of non-twenty-four-hour routines of living on oral temperature and heart rate.* **J. Appl. Physiol.** 6:283.
141. Kleitman, R., and A. Ramsaroon (1948): *Periodicity in body temperature and heart rate.* **Endocrinology** 43:1.
142. Kleitman, N., S. Titelbaum, and P. Feiveson (1938): *The effect of body temperature on reaction time.* **Amer. J. Physiol.** 121:495.
143. Knauth, P., and J. Rutenfranz (1972): *Untersuchungen zum Problem des Schlafverhaltens bei experimenteller Schichtarbeit.* **Int. Arch. Arbeitsmed.** 30:1.
144. Kogi, K., K. Hashimoto, and Y. Saito (1969): *Consecutive night duties and their effects on control task.* XVI Int. Congr. Occup. Health, Tokyo, 108.
145. Kogi, K., and Y. Saito (1971): *Section 3: Assessment criteria for mental fatigue. A factor-analytic study of phase discrimination in mental fatigue* **Ergonomics** 14:119.
146. Kamarov, F.J., A.J. Ivanow, and N.F. Lebedev (1963): *Vliianie kachestvennykh osobennosti uzhina na sostoianiie nochnoi zheludochnoi sekrecii u zdorovykh ludei i bolnykh khronicheskim gastritom.* **Vop. Pit.** 22:6:16.
147. Kozlowski, S. (1970): *Physiology of physical work* (Polish). PZWL. Warszawa.
148. Kreider, M.B., E.R. Buskirk, and D.E. Bass (1958): *Oxygen consumption and body temperature during the night.* **J. Appl. Physiol.** 12:361.
149. Krieger, D.T., and H.P. Krieger (1966): *Circadian variations of the 17-hydroxycorticosteroids in central nervous system disease.* **J. Clin. Endocr.** 26:929.
150: Lafontaine, E., J. Lavernhe, J. Courillon, M. Medvedeff, and J. Ghats (1967): *Influence of air travel east-west and vice versa on circadian rhythms of urinary elimination of potassium and 17-hydroxycorticosteroids.* **Aerospace Medicine** 38:944.
151. Lehmann, G. (1953): *Tagesrhythmik und Leistungbereitschaft.* **Acta Med. Scand.** Suppl. 278, 140.

152. Lehmann, G. (1958): *Effect of environmental factors on biological cycles and performance of work.* In: *Man's Dependance on the Earthly Atmosphere,* K.E. Schaefer, Ed. Macmillan Company, New York, 381.

153. Lehmann, G., and H.F. Michaelis (1941): Die Messung der korperlichen Leistungsfahigkeit. **Arbeitsphysiologie** 11:376.

154. Levi, L. (1970): *Physiological methods of measuring industrial stress.* Occup. Mental Health Notes, 1.

155. Levi, L. (1972): *A synopsis of ecology and psychiatry: Some theoretical psychosomatic considerations, review of some studies and discussion of preventive aspects.* Reports from the Laboratory for Clinical Stress Research, No. 30.

156. Lewinsohn, H.C., L.H. Capel, and J. Smart (1960): *Changes in forced expiratory volume throughout the day.* **Brit. Med. J.** 1:462.

157. Lewis, S.A. (1969): *Sleep pattern during afternoon naps in the young and elderly.* **Brit. J. Psychiatry** 115:107.

158. Lewis, P.R., and M. C. Lobban (1957): *The effect of prolonged periods of life on abnormal time routines upon excretory rhythms in human subjects.* **Quart. J. Exper. Physiol. and Cogn. Med. Sci.** 42:356.

159. Lewis, P.R., and M.C. Lobban (1957): *Dissociation of diurnal rhythms in human subjects living on abnormal time routines.* **Quart. J. Exper. Physiol.** 42:371.

160. Lippold, O.C.J. (1967): *Electromyography.* In: *Manual of Psycho-physiological methods,* P.H. Venables and I. Martin, Eds. North-Holland Publishing Company, Amsterdam.

161. Little, M.A., and J.A. Rummel (1971): *Circadian variation in thermal and metabolic responses to heat exposure.* **J. Appl. Physiol.** 31:556.

162. Lobban, M.C. (1963): *Human renal diurnal rhythms in an Arctic mining community.* **J. Physiol.** 165:75.

163. Lobban, M.C. (1965): *Time light and diurnal rhythms.* In: *The Physiology of Human Survival,* O.G. Edholm and A. L. Bacharach, Eds. Acad. Press, New York and London, 351.

164. Long, B. (1969): *Sleep.* **Amer. J. Nursing** 69, 1896.

165. Luce, G.G., and J. Segal (1966): *Sleep.* Coward-McCann, New York.

166. Macnab, R.B.J., P.R. Conger, and P.S. Taylor (1969): *Differences in maximal work capacity in men and women.* **J. Appl. Physiol.** 27:644.

167. Makowiec-Dabrowska, T., J. Wojtczak-Jaroszowa, and D. Brykalski (1967): *Night and shift work. II. Pulmonary ventilation, oxygen consumption and energy expenditure during shift work.* **(Polish) Med. Pracy** 18,4,340.

168. Makowska, Z. (1974): *Night and shift work. V. Fatigue of women employed at 3-shift system in textile industry, sleep time and preference of different working shift and shift systems.* (Polish) **Med. Pracy** 25:4:321.

169. Makowska, Z., and J. Wojtczak-Jaroszowa (1971): *Manual performance during the day and at night.* (Polish) **Med. Pracy** 22:485.

170. Makowska, Z., and J. Wojtczak-Jaroszowa (1972): *Day-night differences in visual and auditory perception.* (Polish) **Med. Pracy** 23:559.

171. Malinowski, A. (1973): *The influence of shift work on some morphofunctional features.* (Polish) **Zdrowie Publ.** 84:731.

172. Mann, H., E. Poppel, and J. Rutenfranz (1972): *Untersuchungen zur Tagesperiodik der Reaktionszeit bei Nachtarbeit.* **Int. Arch. Arbeitsmed.** 29:269.

173. Mann, H. J. Rutenfranz, and J. Aschoff (1972): *Untersuchungen zur Tagesperiodik der Reaktionszeit bei Nachtarbeit. I. Die Phasonlage des positiven Scheitelwertes und Einffusse des Schlafs auf die Schwingungsbreite.* **Int. Arch. Arbeitsmed.** 29:159.

174. Markiewicz, B., and M. Was-Wojciechowska (1970): *O racjonalna organizacje pracy zmianowej.* **Ochr. Pracy** 21:4:1.

175. Marten, R.,(1955): *24-Stunden-Rhythmus der Urokathepsin und Uropepsin-aussecheidung.* **Acta Med. Scand.** Suppl. 307:192.

176. Martin, M.M., and D.E. Hellman (1964): *Temporal variation in SU-4885 responsiveness in man: Evidence in support of circadian variation in ACTH secretion.* **J. Clin. Endocrin. Metabolism** 24:253.

177. Masterton, J.P. (1965): *Patterns of sleep.* In: *The Physiology of Human Survival.* O.G. Edholm and A. L. Bacharach, Acad. Press., London and New York, 387.
178. McGirr, P.O.M. (1966): *Health consideration in shift working.* PERA Symposium.
179. Meddis, R. (1968): *Human circadian rhythms and the 48-hour day.* **Nature** 218:964.
180. Mellett, H.C., B.K. Hutt, S.I. Askovitz and S.M. Horvath (1951): *Diurnal variation in body temperatures.* **J. Appl. Physiol.** 3:665.
181. Menzel, W. (1950): *Zur Physiologie und Pathologie des Nachtund Schicht-arbeiters.* **Arbeitsphysiologie** 14:304.
182. Menzel, W. (1962): *Menschliche Tag-Nacht-Rhythmik und Schichtarbeit.* Benno-Schwabe und Co., Stuttgart.
183. Metz, B., and J. Schwartz (1949): *Etudes des variations de la temperature rectale, du debit urinaire et l'ecretion urinaire des 17-cetosteroides chez l'homme au cours du nycthene re. Soc. Biol.*, Paris 143:1237.
184. Miani, A., and C. Miani (1973): *Circadian advancement rhythm of the calcification front in dog dentin.* **Pol. Tyg. Lek.** 28:490.
185. Migeon, C.J., F.A.B. Tyler, J.P. Mahoney, A.A. Florentin, H. Castle, E.L. Bliss, and L.T. Samuels (1956): *The diurnal variation of plasma levels and urinary excretion of 17-hydroxycorticosteroids in normal subjects, night workers and blind subjects.* **J. Clin. Endocr. Met.** 16:622.
186. Mills, J.N. (1964): *Circadian rhythms during and after three months in solitude underground.* **J. Physiol.** London 174:217.
187. Mills, J.N., and S.W. Stanbury (1955): *Rhythmic diurnal variation in the behavior of the human renal tubule.* **Acta Med. Scand.** Suppl. 307:95.
188. Moore Ede, M.C., M.H. Faulkner, and B.E. Tredre (1972): *An intrinsic rhythm of urinary calcium excretion and the specific effect of bedrest on the excretory pattern.* **Clin. Sci.** 42:433.
189. Morioka, M. (1969): *Physiological burden to shift workers; A study on their sleeping hours.* XVI Int. Congr. Occup. Health, Tokyo, 101.
190. Mott, P.E., F.C. Mann, Q. McLoughlin, and D.P. Warwick (1965): *Shift Work: The Social, Psychological and Physical Consequences.* Cresset Press, London.
191. Murray, E.J., H.L. Williams, and A. Lubin (1958): *Body temperature and psychological ratings during sleep deprivation.* **J. Exp. Psychol.** 56:271.
192. Nazar, K. (1972): *Circadian variations of physiological functions as a cause of changes in work ability.* (Polish) **Med. Lotnicza,** Warszawa 38:31.
193. Neuberger, F. (1963): *Horschwellencyclus und horschwellenvergleich.* **Acta Otolaryngol.** 56:253.
194. O'Donnel, D.R. (1971): *The internal clock of the international jet traveller.* **Mod. J. of Australia** 23:1227.
195. Ogata, K., and T. Sasaki (1963): *On the causes of diurnal body temperature rhythm in man, with reference to observation during voyage.* **Japan. J. Physiol.** 13:84.
196. Okazaki, S. (1928): *An experimental study of the lack of sleep.* **Ref. in Psychol. Abstr.** 2:628.
197. Oledzka, A. (1967): *Time spent for home duties by working mothers in relation to their whole budget-time.* (Polish) **Biul. IGS** 10:7.
198. Osborne, W.A. (1908): *Body temperature and periodicity.* **J. Physiol.** 36:39.
199. Ostberg, O. (1973): *Interindividual differences in circadian fatigue patterns of shift work.* **Brit. J. Industr. Med.** 30:341.
200. Pasnau, R.O., P. Naitoh, S. Stier, and E.J. Kollar (1968): *The physiological effects of 205 hours of sleep deprivation.* **Arch. Gen. Psychiat.** 18:496.
201. Pawlowska-Skyba, K. J. Wojtczak-Jaroszowa, and M. Romejko (1968): *Night and shift work. III. Influence of 3-shift system upon some physiological functions.* (Polish) **Med. Pracy** 19:321.
202. Pegram, G.V., M.L. Reite, L.M. Stephens, T.J. Crowley, D.F. Buxton, O.F. Lewis, and J.M. Rhodes (1968): *Prolonged sleep deprivation in the monkey: Effects on sleep patterns and brain temperature.* **Psychophysiology** 5:237.
203. Pierach, A. (1955): *Nachtarbeit und Schichtwechsel beim gesunden und kranken Menschen.* **Acta Med. Scand.** Suppl. 307:159.
204. Pittendrigh, S. (1967): *Circadian rhythms, space research and manned space flight.* In: *Life Sciences and Space Research.* North-Holland, Amsterdam, 122.

205. Pradhan, S.M. (1969): *Reaction of workers on night shift.* XVI Int. Congr. Occup. Health, Tokyo, 112.
206. Preston, F.S., and S.C. Bateman (1970): *Effect of time zone changes on the sleep patterns of BOAC B.707 crews on world-wide schedules.* **Aerospace Medicine** 41:1409.
207. Quaas, M. (1969a): *Probleme der Adaptation, Leistungsfahigkeit und Organization der Schichtarbeit in der DDR.* Int. Symposium on Night and Shift Work, Oslo, 112.
208. Quaas, M. (1969b): *Problems of adaptation and organization of shift work in the German Democratic Republic.* XVI Int. Congr. Occup. Health, Tokyo, 105.
209. Quabbe, H.J., H. Helge, and S. Kubicki (1971): *Nocturnal growth hormone secretion: correlation with sleeping EEG in adults and pattern in children and adolescents with non-pituitary dwarfism, overgrowth, and with obesity.* **Acta Endocrin.** 67:783.
210. Radzialowski, F.M., and W.F. Bousquet (1967): *Circadian rhythm in hepatic drug metabolizing activity in the rat.* **Life Sci.** 6:2545.
211. Reil, C. (1822): *Uber die Ausdunstung und die Warmeentwicklung zur Tages- und Nacht-zeit. Wage- und Thermometerversuche.* **Dtsch. Arch. Physiol.** 7:359.
212. Reinberg, A., J. Ghata, F. Halberg, P. Gervais, H. Abulker, J. Dupont, and C. Gaudeau (1970): *Rhythmes circadiens du pouls, de la pression arterialle, des excretions urinaires en 17-hydroxycorticosteroides catecholamines et potassium chez l'homme adulte sain, actif et au repos.* **Ann. d'Endocrin.** 31:277.
213. Reinberg, A., F. Halberg, J. Ghata, and P. Gervais (1969): *Rhythme circadian de diverses fonctions physiologiques de l'homme adulte sain, actif et au repos pouls, pression arterielle, excretion urinaires des 17-OHCS, des catecholamines et du potassium.* **J. de Physiol.** Suppl. 2:61.
214. Reinberg, A. and E. Sidi (1966): *Circadian changes in the inhibitory effects of an antihistaminic drug in man.* **J. Invest. Dermatol.** 46:415.
215. Reinberg, A., Z.W. Zagula-Mally, J. Ghata, and F. Halberg (1967): *Circadian rhythm in duration of salicylate excretion referred to phase of excretory rhythms and routine.* **Proc. Soc. Exp. Biol. Med.** 124:826.
216. Reite, M., V. Pegram, and C. Todd (1968): *EEG changes during sleep deprivation in the monkey.* **Psychophysiology** 5:240.
217. Richardson, D.W., A.J. Honour, G.W. Fenton, F.H. Stott, and G.W. Pickering (1964): *Variation in arterial pressure throughout the day and night.* **Clin. Sci.** 26:447.
218. Rutenfranz, J., J. Aschoff, and H. Mann (1972): *The effects of a cumulative sleep deficit, duration of preceding sleep period and body temperature on multiple choice reaction time.* In: *Aspects of Human Efficiency,* W.P. Colquhoun, Ed. English Universities Press, Ltd., London, 217.
219. Rutenfranz, J., and P. Knauth (1971): *Investigation of the problems concerning the influence upon sleep of shift workers.* Proc. Second Int. Symposium on Night and Shift Work, Slanchev Bryag, 58.
220. Rutenfranz, J., H. Mann, and J. Aschoff (1969): *Circadian rhythmik physischer und psychischer Funktionen bei 4-stundingen Wachwechsel auf einem Schift.* Int. Symposium on Night and Shift Work, Oslo, 31.
221. Rzepecki, H., and J. Wojtczak-Jaroszowa (1969): *Night and shift work. II. Variations in physiological tests performed by shift workers at different time of day.* **Med. Pracy** 20:1:40.
222. Saito, S., and K. Takagi (1973): *Studies on the effect of shift work on the meal time.* **J. Science of Labour** 49:667.
223. Samol, S. (1966): *Some psychological and sociological problems of work.* **Biul. Inform.** 2:55.
224. Sampson, H. (1965): *Deprivation of dreaming sleep by two methods.* **Arch. Gen. Psychiat.** 13:79.
225. Sasaki, T. (1972): *Circadian rhythm in body temperature.* In: *Advances in Climatic Physiology.* S. Itoh, Ed. Igaku Shoin Ltd., Tokyo.
226. Sasaki, T., and L.D. Carlson (1964): *Effect of a sleep change in temperature on skin temperature and blood flow.* **Proc. Soc. Exp. Biol. Med.** 117:334.
227. Sassin, J.F., D.C. Parker, J.W. Mace, R.W. Gotlin, L.C. Johnson, and L.G. Rossman (1969): *Human growth hormone release: relation to slow-wave sleep and sleep-waking cycles.* **Science** 165:513.
228. Schubert, D.S.P. (1969): *Simple task rate as a direct function of diurnal sympathetic nervous system predominance.* **J. Comparat. and Physiological Psychology** 68:434.

229. Schunch, K.H. (1957): *A new shift system and its effect on status of illnesses, accidents and on free time.* XII Int. Congr. Occup. Health, Helsinki, II. 36.
230. Scollo-Lavizzari, G., P. Levin, and G. R. Scollo-Lavizzari (1972): *Photoconvulsive responses and sleep deprivation.* In: *Sleep,* W.P. Koella, Ed. Basel, 528.
231. Soligman, S.A. (1971): *Diurnal blood pressure variation in pregnancy.* **Journ. of Obst. and Ginaecol. of the Brit. Commonwealth** 78:417.
232. Simmons, D.J., and G. Nichols (1966): *Diurnal periodicity in the metabolic activity of bone tissue.* **Am. J. Physiol.** 210:411.
233. Simpson, H. (1965): *The daily rhythm in equatorial Amerindians.* **J. Endocrin.** 32:179.
234. Smith, R.E. (1969): *Circadian variation in human thermoregulatory responses.* **J. Appl. Physiol.** 26:554.
235. Smolensky, H., F. Halberg, and F. Sargent (1972): *Chronobiology of the life sequence.* In: *Advances in Climatic Physiology,* S. Itoh, Ed. Igaku Shoin Ltd., Tokyo.
236. Soloveva, W.P., and G.M. Gambashidze (1960): *Fizjologicheskoie obosnovaniie rezhima truda i otdykha pri postoiannoi rabote v nochnuiu smenu.* **Gig. Truda** 7:17.
237. Stanbury, S.W., and A.E. Thomson (1951): *Diurnal variations in electrolyte excretion.* **Clin. Sci.** 10:267.
238. Strughold, H. (1952): *Physiological day-night cycle in global flights.* **J. Aviat. Med.** 23, Suppl. 80.
239. Szczepanska, E., J. Prejbisz, K. Drzewiecki, and S. Kozlowski (1967): *Dobowy rytm wahan poziomu hormonu antyoiuretycznego we krwi u ludzi.* **Pol. Arch. Med. Wewn.** 39:475.
240. Takagi, K. (1970): *Physiological and bibliographical considerations on the meals of shift workers and the habit of working without breakfast.* **J. Sci. Lab.** 46:639.
241. Takagi, K., S. Koizumu, and N. Takagi (1967): *Studies on the effect of shift work on the meal-time.* **J. Sci. Lab.** 43:520.
242. Takebe, K., and M. Sakakuza (1972): *Circadian rhythm in pituitary-adrenocortical function.* In: *Advances in Climatic Physiology.* S. Itoh, Ed. Igaku Shoin Ltd., Tokyo.
243. Taylor, P.J. (1969): *The problems of shift work.* Proc. Int. Symposium on Night and Shift Work, Oslo, 15.
244. Taylor, P.J. (1970): *Shift work — some medical and social factors.* **Trans. Soc. Occup. Med.** 20:127.
245. Taylor, P.J., S.J. Pocock, and R. Sergean (1972): *Shift and day workers absence: relationship with some terms and conditions of service.* **Brit. J. Industr. Med.** 29:338.
246. Teleky, L. (1943): *Problems of night work: Influences on health and efficiency.* **Ind. Med. Surg.** 12:758.
247. Thiis-Evensen, E. (1957): *Shift work and health.* XII Int. Congr. Occup. Health, Helsinki, 97.
248. Thiis-Evensen, E. (1958): *Shift work and health.* **Ind. Med. Surg.** 27:493.
249. Thiis-Evensen, E. (1969): *Shift work and health.* Proc. Int. Symposium on Night and Shift Work, Oslo, 81.
250. Toulouse, E., and H. Pieron (1907): *Le mechanisme de l' inversion chez l'homme du rhythme nycthemeral de la temperature.* **J. Physiol. Path. Gen.** 9:425.
251. Tsaneva, N., E. Dincheva, and N. Stoyanova (1971): *Changes of work capacity at night, evaluation of the maximum working capacity MWC.* Proc. Second Int. Symposium on Night and Shift Work. Slanchev Bryag, 79.
252. Tune, G.S. (1968): *The human sleep debt.* **Sci. J.** 4:67.
253. Tune, G.S. (1969): *Sleep and wakefulness in a group of shift workers.* **Brit. J. Industr. Med.** 26:54.
254. Valentin, H., W. Klosterkotter, G. Lahnert, H. Petry, J. Rutenfranz, and H. Wittgens (1971): *Arbeitzmedizin.* Georg Thieme Verlag, Stuttgart.
255. van Loon, A.H. (1963): *Diurnal body temperature curves in shift workers.* **Ergonomics** 6:267.
256. Vernon, H.M. (1918): *An investigation of the factors concerned in the causation of industrial accidents.* Health of Munition Workers Committee, Memo 21, Cd. 9046, H.M.S.O., London.
257. Voight, E.D., P. Engel, and H. Klein (1967): *Tagesrhytmische Schwankungen des Leistungspuls-Index.* **Germ. Med. Mtgh.** 17:394.
258. Voight, E.D., P. Engel, and H. Klein (1968): *Uber den Tagesgang der korperlichen Leistungfahigkeit.* **Int. Z. Angew. Physiol. Einschl. Arbeitsphysiol.** 25:1.

259. Wahlberg, J., and I. Astrand (1973): *Physical work capacity during the day and at night.* **Work Environ. Hlth.** 10:65.
260. Walford, I., B. Lammers, R. S. F. Schilling, D. van den Hoven van Genderen, and Y.G. van der Veen (1966): *Diurnal variation in ventilatory capacity. An epidemiological study of cotton and other factory workers employed on shift work.* **Brit. J. Industr. Med.** 23:142.
261. Walker, J. (1966): *Frequent alternation of shifts on continuous work.* **Occup. Psychol.** 40:215.
262. Wasiliew, J.G., L.P. Zimnickaja, E.L. Skljarcyk, K.M. Smirnov, B.G. Filipov, S.A. Chitun, and A.M. Szatalov (1957): *O sutochnom ritmo rabotosposobnosti cheloveka.* **Fizjol. Zhurn** 43:817.
263. Webb, W.B. (1971): *Sleep behavior as a biorhythm.* In: *Biological Rhythms and Human Performance,* W.P. Colquhoun, Ed. Acad. Press, London and New York.
264. Webb, W.B. (1972): *Pattern of sleep behaviour.* In: *Aspects of Human Efficiency,* W.P. Colquhoun, English Universities Press Ltd., London, 31.
265. Webb, W.B., and H.W. Agnew (1965): *Sleep: Effects of a restricted regime.* **Science** 150:1745.
266. Webb, W.B., and H.W. Agnew (1967): *Sleep cycling within 24-hour periods.* **J. Exp. Psychol.** 74:158.
267. Webb, W. B., H.A. Agnew, and R.L.W. Williams (1971): *Effect on sleep of a sleep period time displacement.* **Aerospace Medicine** 42:152.
268. Webb, W.B., and H. Swinburne (1971): *An observational study of sleep of the aged.* **Percept. Mot. Skills** 32:895.
269. Wedderburn, A.A.Z. (1967): *Social factors in satisfaction with swiftly-rotating shifts.* **Occup. Psychol.** 41:85.
270. Wedderburn, A.A.I. (1971): *Sleep patterns on the 25-hour day in a group of tidal shiftworkers.* Proc. of the Second Inter. Symposium on Night and Shift Work, Slanchev Bryag, 101.
271. Weitzman, E.D., D. Goldmacher, D. Kripke, P. McGregor, J. Kream, and L. Hellman (1968): *Reversal of sleep-wake cycle: effect on sleep stage pattern and certain neuroendocrine rhythms.* **Trans. Amer. Neurol. Assoc.** 93:153.
272. Weitzman, E.D., D. Kripke, D. Goldmacher, P. McGregor, and C. Nogeire (1970): *Acute reversal of the sleep-waking cycle in man.* **Arch. of Neurol.** 22:483.
273. Wilkinson, R.T. (1964): *Effects of up to 60-hours sleep deprivation on different types of work.* **Ergonomics** 3:175.
274. Wilkinson, R.T. (1969): *Sleep deprivation: Performance tests for partial and selective sleep deprivation.* Progress in Clin. Psychol., Grune, and Stratton, Inc., 28.
275. Wilkinson, R.T. (1972): *Sleep deprivation.* In: *The Physiology of Human Survival,* O. G. Edholm and A. L. Bacharach, Eds. Acad. Press, London and New York, 399.
276. Wojtczak-Jaroszowa, J. (1971): *Changes in manual performance and physical fitness in day and night.* Proc. Second Int. Symposium on Night and Shift Work, Slanchev Bryag, 107.
277. Wojtczak-Jaroszowa, J. (1973a): *Physiological cost of physical work performed at night.* **Med. Pracy** 24:17.
278. Wojtczak-Jaroszowa, J. (1973b): *Some Physiological aspects of night and shift work.* **Med. Pracy** 24:1.
279. Wojtczak-Jaroszowa, J., A. Banaszkiewicz, and T. Makowiec-Dabrowska (1971): *Variations in physiological reactions to physical exertion in relation to the time of day.* Symposium, Bialowieza, 173.
280. Wojtczak-Jaroszowa, J., and A. Banaszkiewicz (1974): *Physical work capacity during day and night.* **Ergonomics** 17:2:193.
281. Wojtczak-Jaroszowa, J., and Z. Maciaszek (1971): *Electromyographical analysis of reaction time.* **Acta Neurobiol. Exp.** 31:141.
282. Wojtczak-Jaroszowa, J., Z. Maciaszek, and K. Jarosz (1975): *a. Electromyographical analysis of the causes of nightly deterioration of manual performance; b. Experimental model for examination of day-night differences in manual performance.* Symposium on Physiological and Psychological Problems of Automatic Work and Environmental Aspects, Poznan, Poland.
283. Wojtczak-Jaroszowa, J., and K. Pawlowska (1964): *Influence of shift work upon circadian fluctuations of some physiological functions.* (Polish) Symposium on Industrial Medicine, Katowice, Poland.

284. Wojtczak-Jaroszowa, J., and K. Pawlowska (1965): *Effect of shift work upon physiological functions.* (Polish) VII National Conference of Industrial Medicine Poznan, Poland.
285. Wojtczak-Jaroszwa, J., and K. Pawlowska-Skyba (1967): *Night and shift work. I. Circadian variations in work* (Polish) **Med. Pracy** 18:1.
286. Wusthoff, R. (1960): *Schichtarbeit und Diabetes.* **Der Bahnarzt** 7:295.
287. Wyatt, S., and R. Marriott (1953): *Night work and shift changes.* **Brit. J. Industr. Med.** 10:164.
288. Wyrwick, W., and A. Duncan (1970): *Within-day trends of motor latency and nerve conduction velocity in males and females.* **Amer. J. Phys. Med.** 49:307.
289. Yoshimura, H., and T. Morimoto (1972): *Seasonal and circadian variations in body fluid.* In: *Advances in Climatic Physiology,* S. Itoch, K. Ogata, and H. Yoshimura, Eds. Igaku Shoin Ltd., Tokyo, 381.
290. Yoshitake, H. (1971): *On the variation of frequency of subjective fatigue symptoms.* **J. Sci. Lab.** 47:383.

ADDENDUM

CHAPTER VII

SOME PHYSIOLOGICAL ASPECTS OF CIRCADIAN VARIATIONS IN GLUCOSE TOLERANCE

In recent years, the interest in circadian variations of glucose tolerance has greatly increased. Because these variations may determine at least to some extent the course and range of diurnal periodicity in the capability to perform physical work, as mentioned in Chapter II, some attention should be given to this problem.

Circadian variations in the several hormones which have an effect on carbohydrate metabolism have been described in Chapters I and II. Among others, the growth hormone (HGH) which is important in carbohydrate and lipids metabolism, has been suspected of playing a basic role in the diurnal fluctuations of carbohydrate metabolism. The relationships between the diurnal variations of HGH secretion and those of glucose tolerance have been examined and no cyclic variations over a 24-hour period were found (4,8,10,20,22,23). The level of HGH in peripheral blood did not differ in the morning and evening in fasting men, and no diurnal variations in plasma HGH were observed after both oral and intravenous glucose administration. An elevation of HGH levels was noted in response to insulin induced hypoglycemia in the evening but not in the morning (4).

No close correlation has been detected between peak secretion of HGH and levels of plasma free fatty acids (FFA). The 24-hour curves of blood sugar, FFA, HGH, and insulin during fasting in healthy adults studied by Quabbe, Schilling, and Helge (18) are presented in figures 1 and 2. The fact that the peak secretion of HGH seems independent of changes in the concentration of blood sugar or FFA, suggests that neither is directly responsible for stimulation or inhibition of the release of HGH under conditions of total starvation.

The indubitable connection of HGH release and the onset of sleep, rather than with time of day and of meals, has been demonstrated (figs. 3, 4). A clear relationship between HGH peaks and the stages of sleep was described by Takahashi, Kipnis, and Daughaday (20). They examined eight healthy young adults (20 to 30 years old) during normal, as well as, disturbed night sleep. The plasma HGH, blood insulin, cortisol, and glucose levels were measured during 38 nights with simultaneous recordings of EEG and EOG. The results are presented in figure 5 where plasma HGH, glucose, insulin, and cortisol levels have been plotted together from the time sleep commenced. The clear relationship of HGH release with the onset of sleep is seen in figure 6 where the levels of sleep have been recorded during normal night sleep in a 27-year-old man. The highest defined peak of plasma HGH was noted after the onset of sleep, whereas, the cortisol level was low

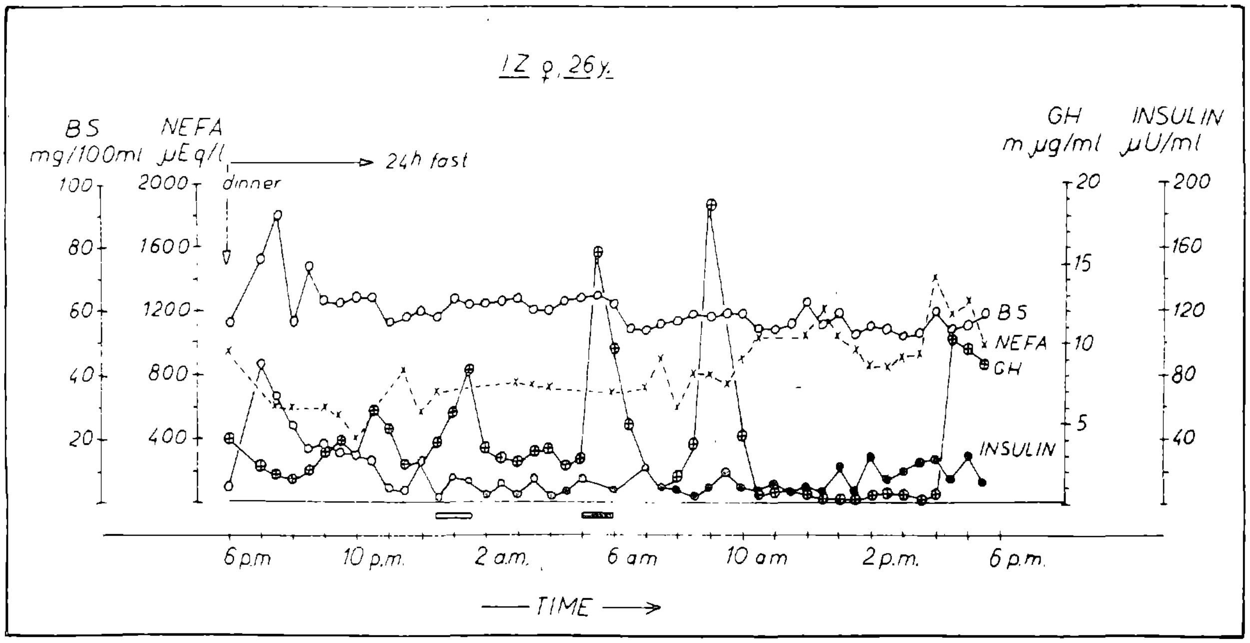


Figure 1. Blood sugar, NEFA, HGH, and insulin (radioimmuoassay) during a 24-hour fast in a normal female. The base line is drawn at the threshold of sensitivity of this individual HGH assay. Heavy bar underlines indicate periods of deeper sleep (Quabbe, Schilling, and Helge, 1966).

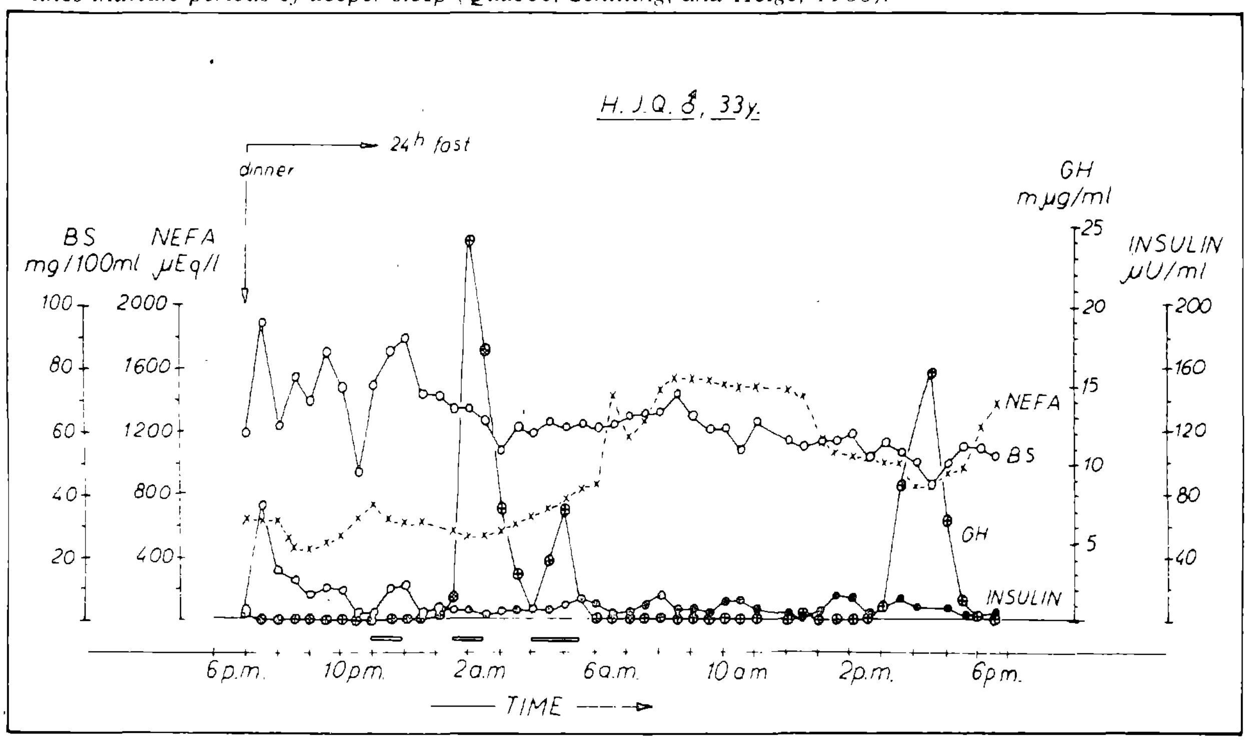


Figure 2. Blood sugar, NEFA, HGH, and insulin (radioimmuoassay) during a 24-hour fast in a normal male. Base line and heavy bars as in Figure 1 (Quabbe, Schilling, and Helge, 1966).

at that time. On the contrary, upon awakening, when cortisol level was at its highest, the plasma HGH level was low.

With the data presented in Chapter V, it should be mentioned that when the onset of sleep is delayed (fig. 7) or when sleep is interrupted (fig. 8), the diurnal pattern of cortisol secretion is disturbed, but HGH release is always connected with the beginning of the sleep. However, the changes in HGH level are not correlated with the changes in plasma glucose and insulin levels.

Convincing data indicate that insulin secretion undergoes cyclic fluctuations over a 24-hour period, which is probably all important for the diurnal changes of carbohydrate metabolism (5,6,14,16,19). First of all, it has been shown that

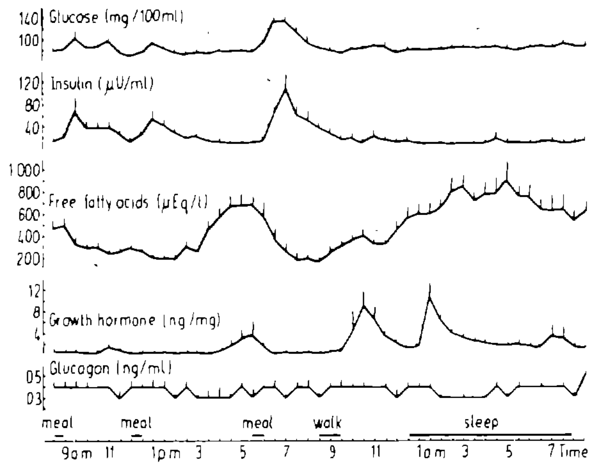


Figure 3. Average curves of blood glucose, serum insulin, free fatty acids, growth hormone, and glucagon in five healthy males. Mean values ± SE (Hansen and Johansen, 1970).

the plasma insulin response to identical meals consumed at different times of the day, was greatest after the morning meal (16,19). Thus, Malherbe et al. (16) examined healthy subjects when the same meal was given in the morning, at midday, and at night. They observed that during the night, blood sugar and plasma insulin remained low, FFA decreased, and the excretion of catecholamines diminished. The morning-midday blood sugar values were not significantly different, whereas the plasma insulin was highest after the morning meal. This was the cause of the changes in the plasma insulin/blood sugar ratio (I/G ratio), which is commonly used to express the insulin response of B-cells to glycemic stimuli. It has been shown that the I/G ratio, like insulin, was maximal in the morning (fig. 9), suggesting that there is an inherent rhythm in the release of insulin from the pancreas.

Similar observations were reported by Rigas et al. (19), who compared the responses to a standard meal in groups of normal subjects, diabetic patients treated with different drugs, and obese subjects on total starvation (fig. 10). The greatest insulin response was consistently observed after the first (morning) of the three equal meals of the day.

These data suggest that the synthesis and the storage of insulin proceeds at a higher level at night than in the day, when the period between meals is shorter. If this is the main mechanism of the described diurnal variations, it seems that a reversal to a morning state of better glucose tolerance might occur during the night, and also during the day, as a result of meal spacing.

For comparison of the relationship between glucose and insulin levels according to the time of day, 11 healthy young men (soldiers) volunteered for studies after prior screening to exclude those with occult diabetes mellitus, hepatic diseases, cardio-renal abnormalities, and endocrinopathies. The subjects were examined during 3 and 4 day periods of total starvation (Freinkel, Mager, and Vinnick, 6). It was observed that plasma glucose progressively declined to a new plateau during starvation but diurnal patterns were not demonstrated. However, plasma immunoreactive insulin levels were significantly greater in the morning (7 a.m. to 8 a.m.) than in the midafternoon (3 p.m. to 4 p.m.) Consistently higher I/G ratios in morning tests resulted from a higher insulin level in the peripheral blood at a given concentration of glucose in the early morning than in the midafternoon. Thus, the diurnal fluctuation of insulin level in the blood cannot be explained as a response only to an increased blood glucose level. The authors related the findings to the possible existence of a periodicity which would regulate insulin secretion independently of any exogenous stimuli evoking insulin release.

As a result of the differences in plasma insulin levels, these diurnal variations in glucose tolerance have been observed. These diurnal variations in oral glucose tolerance tests (OGTT) have been described by many authors (3,4,13,17, 21,23). It has been shown that the blood sugar levels are higher in afternoon and evening tests than in morning tests at all time points, except fasting and 30 minutes after the glucose load (figs. 11, 12). The peak glucose response occurred later in the evening and afternoon tests than in the morning tests. On the contrary, the plasma insulin levels (fig. 13) are lower at 50 minutes in the afternoon and evening than in the morning, whereas at 120 to 180 minutes they are higher in the afternoon (13). In figure 14, the levels of blood glucose, plasma insulin, HGH, and FFA after oral glucose administration have been presented for both morning (7 a.m.) and evening (7 p.m.). These results were obtained by Carroll and Nestel (4) in healthy subjects.

Because the insulin release after oral glucose can be influenced by intestinal factors and these factors might be partly responsible for diurnal variations in glucose tolerance, the response to intravenous glucose administered at different times of the day was also studied (4,10,22).

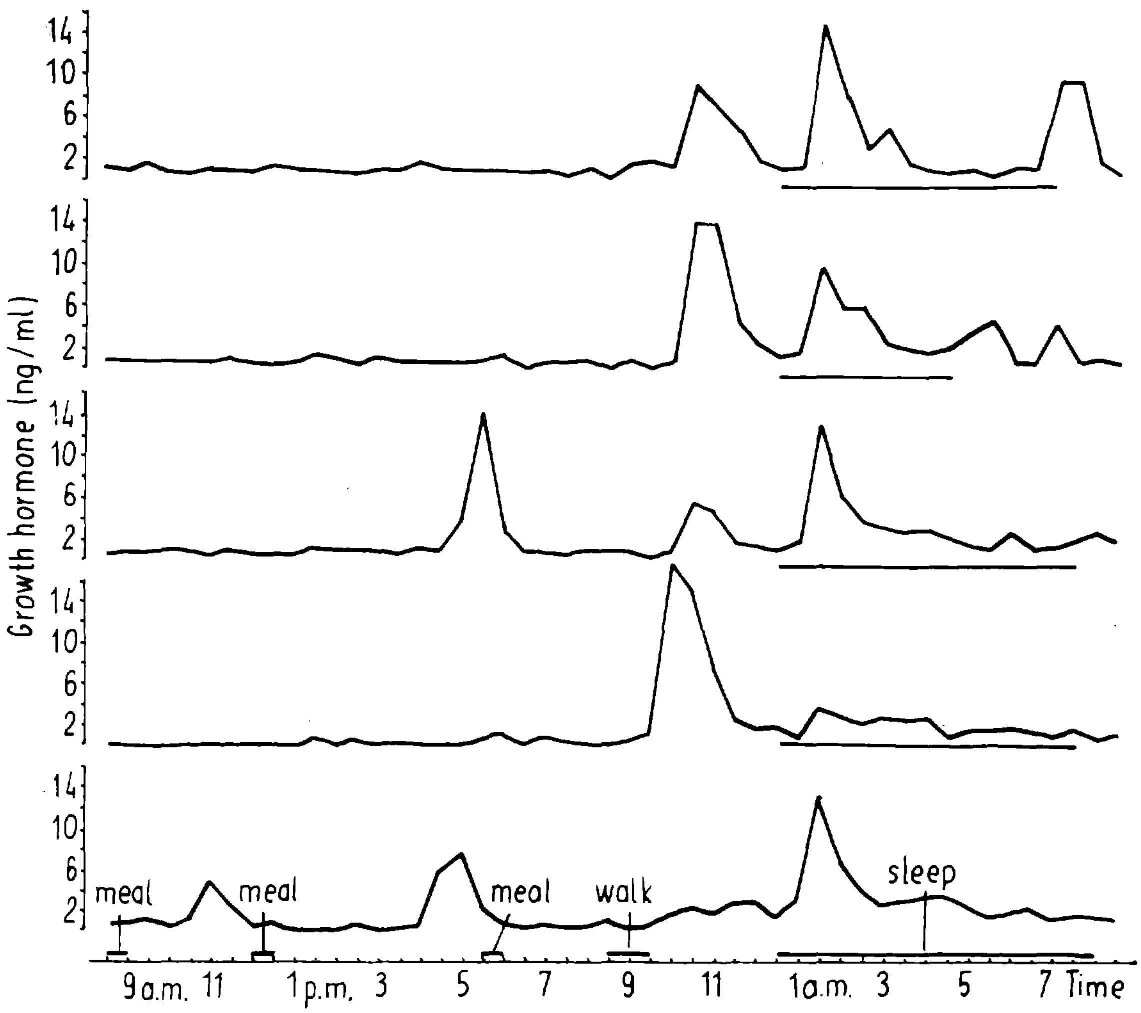


Figure 4. The 24-hour serum growth hormone level in five healthy males (Hansen and Johansen, 1970).

The same direction of diurnal changes were observed when intravenous glucose tolerance tests (IGTT) were used. The differences in the levels of blood glucose and plasma insulin between morning and afternoon tests performed in apparently normal people (Whichelow et al., 22) are presented in figures 15 and 16. Similar results were obtained by Carroll and Nestel (4). Changes in blood sugar during IGTT are shown in figure 17 together with the curves of plasma HGH, insulin, and FFA levels. It was noted that blood glucose concentration was nearly the same in the morning and evening tests at about 10 minutes after glucose injection. Consequently, the curves of both tests showed no difference in the height and timing of the peak level. However, the subsequent rate of glucose disappearance from the blood was significantly slower in the evening, resulting in a more rapid fall after the peak in the morning.

Thus, apparently normal people may show a small diurnal cycle in their response to glucose administration, spending much of the day in a state of relative hyperglycemia. Lestradet and Deschamps (15) analysed the individual results obtained in apparently healthy children before puberty, and found that only one value in one subject could have been regarded as abnormal in the morning tests, whereas 6 out of 10 subjects showed some abnormalities in the afternoon tests.

The statement that the slight degree of glucose intolerance in the afternoon exists in healthy people is also of considerable importance for clinical examinations, because it indicates that glucose

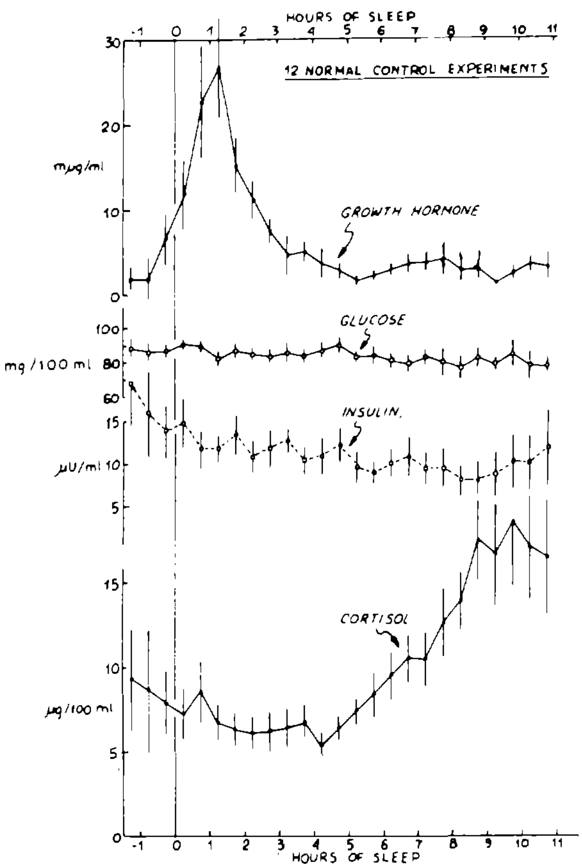


Figure 5. The plasma growth hormone, glucose, insulin, and cortisol levels during 12 normal control sleep studies. All values represent mean ± SE (Takahashi, Kipnis, and Daughaday, 1968).

tolerance tests performed after an overnight fast are not very reproducible when they are performed at different times of the day. Nevertheless, little attention is usually given to the time of day when the tests are carried out. The pattern of glucose and insulin levels for the afternoon and evening tests may resemble the pattern described as typical for "maturity onset diabetes." It has been suggested that afternoon glucose intolerance may represent a high factor of risk in the development of diabetes mellitus (3), and even though the hypothesis has not been confirmed, the investigations in this field seem to be important in understanding the etiology of diabetes. A relatively hyperglycemic response in the afternoon is regarded as a normal phenomenon that occurs in most normoglycemic people.

On the other hand, the investigations of diabetic and obese subjects in which glucose tolerance tests were repeated at different times of the day, contributed to the knowledge of the mechanisms supporting the observed variations. The diurnal variations in blood sugar, plasma insulin, and FFA levels in hyperglycemic individuals were studied by several authors (4,5,8, 11,12,17,19). It has been noted that the degree of diurnal variations was significantly and inversely related to the degree of obesity (12,17). No diurnal variations in both oral and intravenous glucose tolerance test were demonstrated for the people who had virtually no increase in plasma insulin concentration after glucose administration (4).

Jarrett and Keen (12) studied 122 male volunteers (40 or more years old) who participated in a screening health examination. The people were categorized according to the 2-hour blood sugar level in a morning test. Then the OGTT was performed in the morning and afternoon. The results are presented in figure 18.

It is also characteristic that diurnal variations in fasting blood sugar levels in established diabetics are observed with clear peak levels occurring in the morning; such fluctuations are absent in healthy subjects (5,6).

There is insufficient data to explain the mechanisms of glucose intolerance in diabetics. The working hypothesis presented by Jarrett and Keen (12) was that "afternoon hyperglycemia is the first stage of glucose intolerance, followed by increased morning glycemia (and reduced diurnal variation), then proceeding to morning hyperglycemia, sufficient eventually to warrant the description of diabetes mellitus."

Some slight age effects have been detected (13,15,23). Lestradet, Deschamps, and Giron (15) studied 20 normal children before puberty, 8 to 13 years old. Lower blood sugar values during OGTT were noted in the morning, whereas at the same time the insulin response to glucose administration was less rapid in the afternoon than in the morning (fig. 19). Consequently the I/G ratio calculated for morning and afternoon tests was significantly different, suggesting that the β-cells were more sensitive to glucose in the morning hours (fig. 20). Circadian variations in I/G ratio plotted with diurnal fluctuation in urinary excretion of potassium are presented in figure 21. The comparison of the results obtained for a group of children with those obtained for the adults showed that the diurnal variations in OGTT were greater for the adults (15).

Zimmet et al. (23) studied adults between the ages of 22 and 65. The people were divided into two groups, one between 22 and 44 and the other between 45 and 65 years. There were no significant differences in the morning blood sugar levels

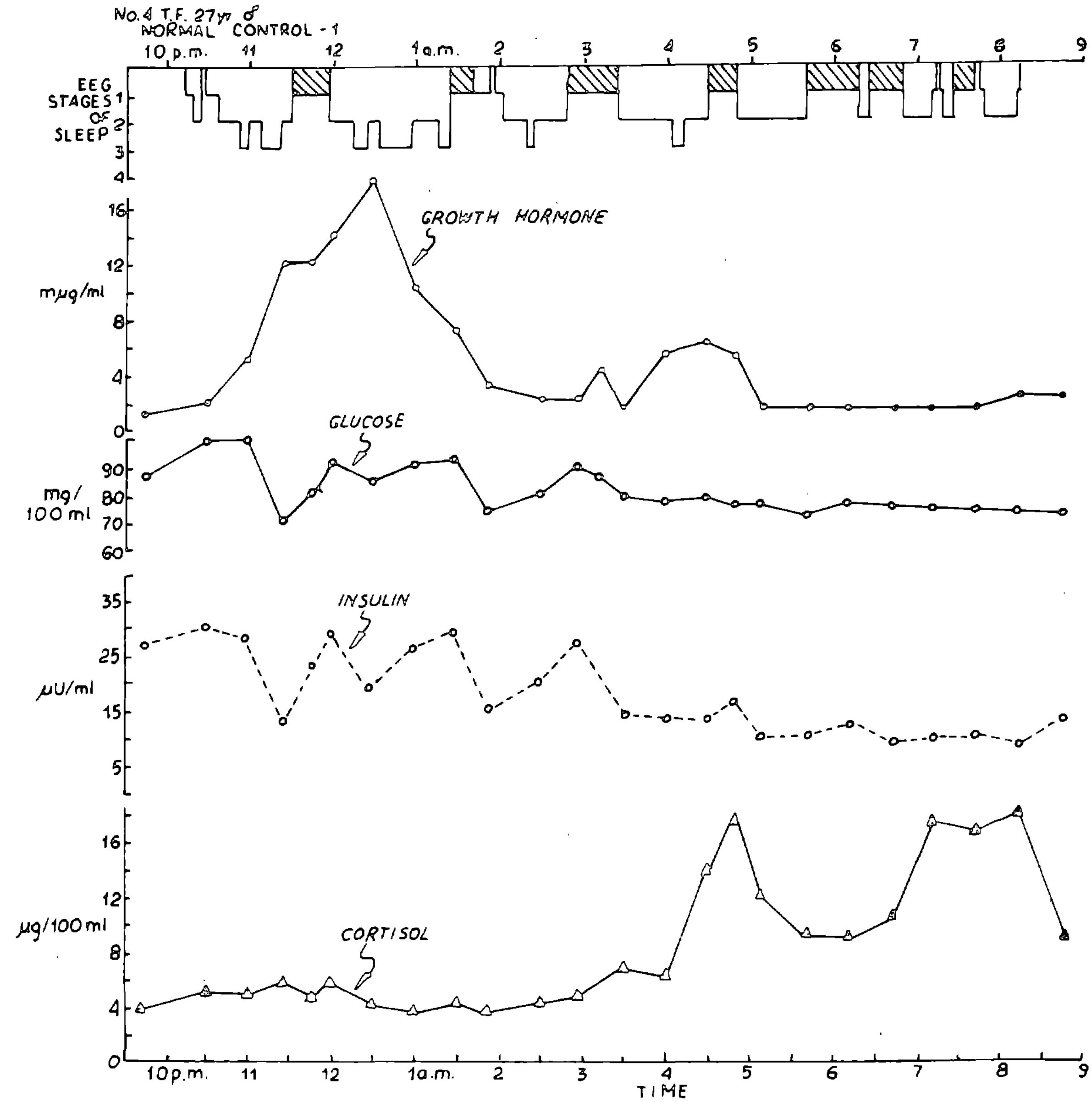


Figure 6. The plasma growth hormone, glucose, insulin, and cortisol levels and EEG-EOG monitored CNS activity during a normal night's sleep in a 27-year-old man. The levels of sleep are indicated at the top of the figure and cross-hatched areas are periods of rapid eye movement (Takahashi, Kipnis, and Daughaday, 1968).

between the two groups. The variations between morning and afternoon tests showed the same pattern for both groups; however, the older group had significantly higher postglucose blood sugar levels at 90, 120, and 150 minutes in the afternoon (fig. 22). Consequently, the range of the diurnal variations was greater for the older subjects. These results did not confirm the previous observations made by Jarrett et al. (13), who found less variations in OGTT in elderly people. The authors attributed this phenomenon to the poorer glucose homeostasis in the elderly rather than to age per se.

The mechanisms behind the diurnal rhythm in glucose tolerance are still unclear. As was mentioned previously, it can not be attributed to HGH fluctuations. The hypothesis that the HGH fluctuations might be the cause of variations in insulin resistance has been unsupported. There are probably numerous mechanisms responsible for the diurnal variations in carbohydrate metabolism.

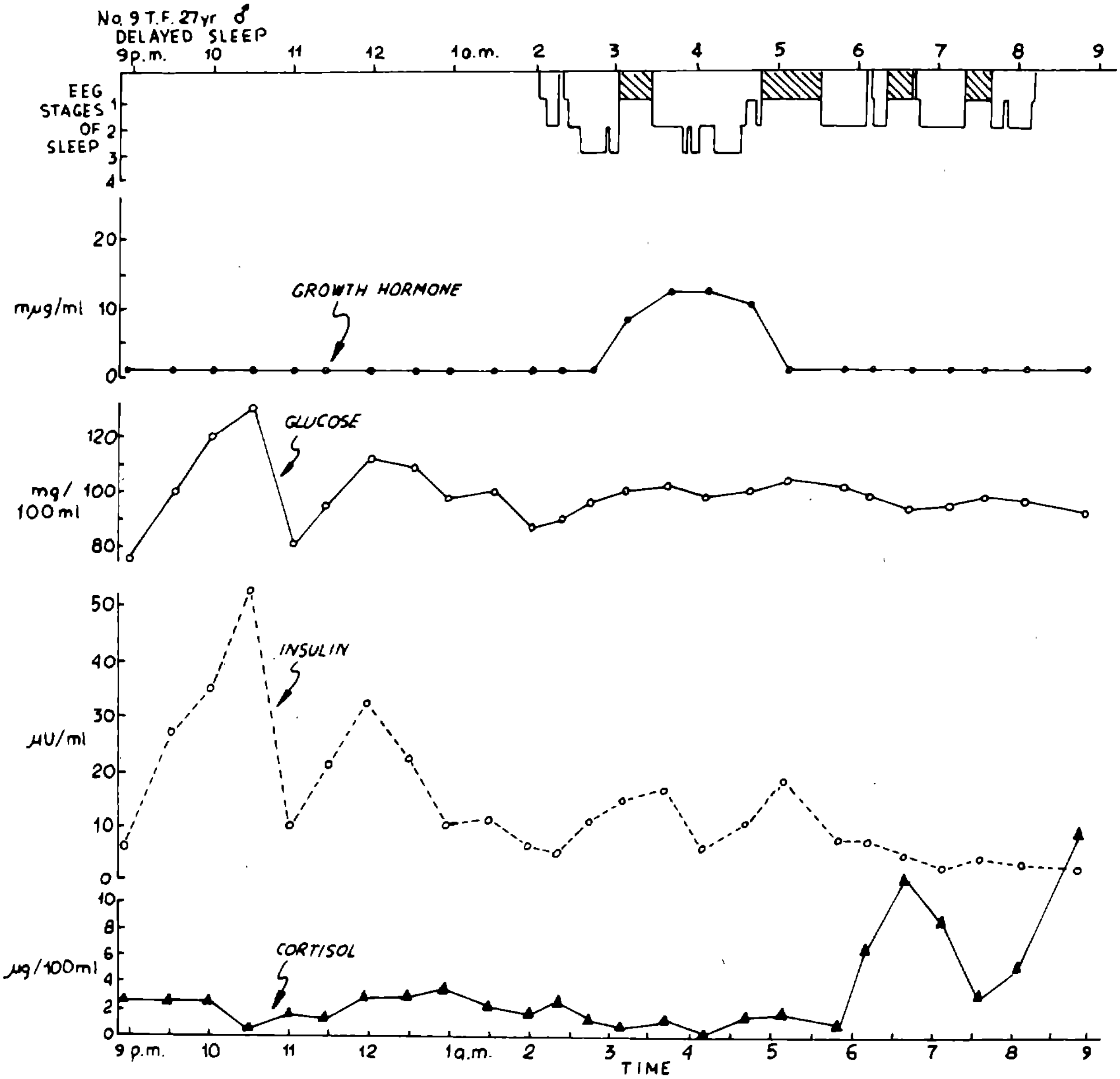


Figure 7. The effect of delaying the onset of sleep on the plasma growth hormone secretory pattern (Takahashi, Kipnis, and Daughaday, 1968).

The following two mechanisms are most frequently considered. The first is associated with a reduction of the hypoglycemic effect of insulin. It is suggested that the diurnal changes in sensitivity of the tissues to endogenous insulin contribute partly to the differences in blood sugar responses (1,7). Some hormones and metabolites such as corticosteroids and FFA would be involved in this process. The circadian variations in plasma cortisol, which is well known for its role in carbohydrate metabolism, were described in Chapter I. The fasting levels of plasma FFA also reveal changes over a 24-hour period. It was found, that during starvation, plasma FFA was significantly higher in the afternoon and evening than in the morning (2,4,22,23). The concentration of triglycerides also increased overnight (2). It might be that a higher level of plasma FFA, with consequent rise of muscle metabolism of FFA, results in reduced insulin sensitivity. However, there are rather controversial data concerning the diurnal variations in insulin tolerance tests. Gibson and Jarrett (7) observed a consistantly and significantly greater fall in blood sugar after morning intravenous insulin. No diurnal variations were seen by Carroll and Nestel (4) whose data are presented in figure 23.

The second explanation is associated with a

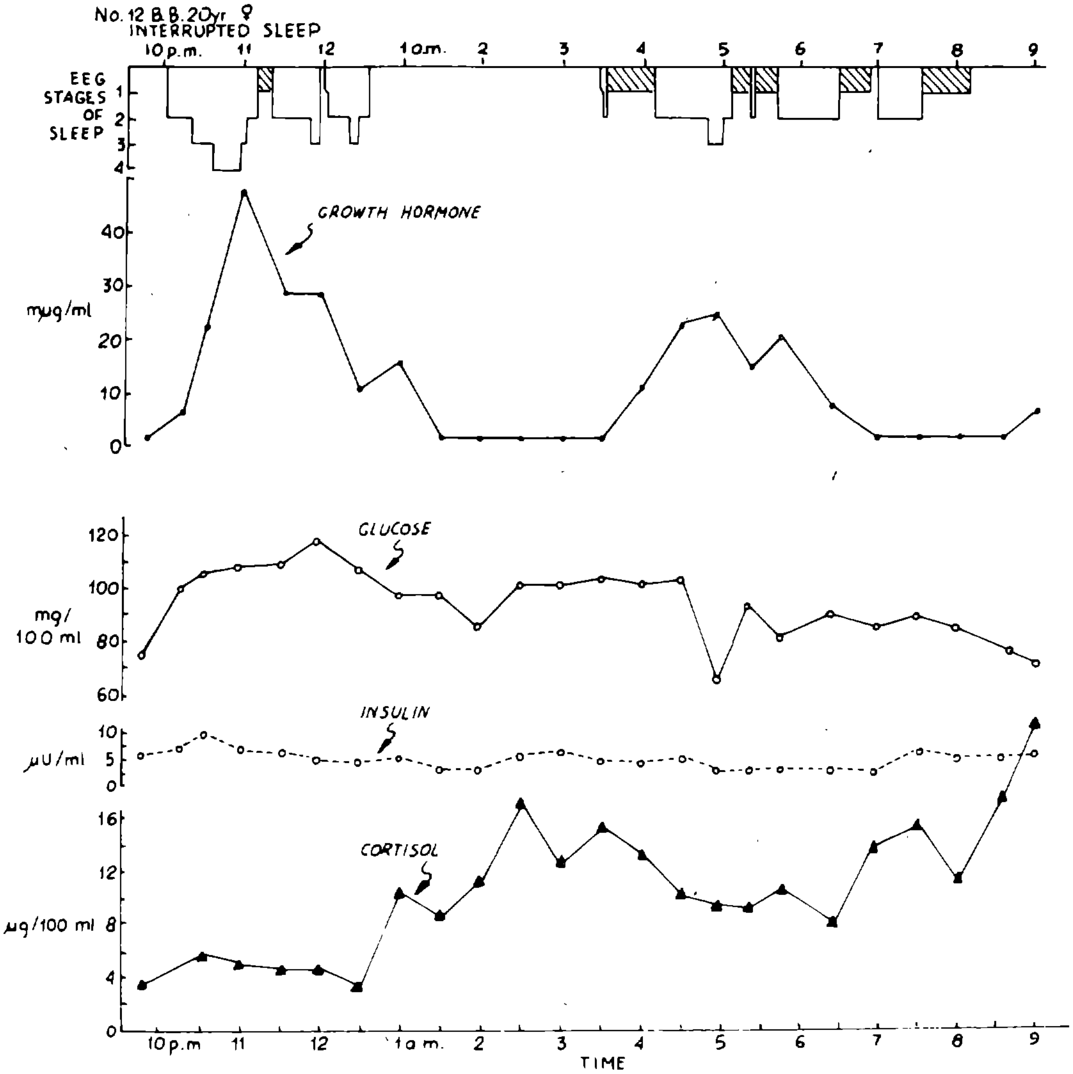


Figure 8. The effect of a 3-hour interruption of sleep on the plasma growth hormone secretory pattern (Takahashi, Kipnis, and Daughaday, 1968).

reduced and delayed output of insulin from the pancreas in the evening. According to this hypothesis, the diurnal variation in glucose tolerance is secondary to a rhythm in islet cell activity which determines the amount of insulin released by the pancreas in response to a given stimulus. The existence of a diurnal variation in nuclear size of the islet cells, not only β-cells but also α-cells, has been demonstrated in experiments on animals (9). A biphasic diurnal curve for the size of the nuclei of the β-cells and a monophasic curve the size of nuclei of the β-cells have been shown for rats (fig. 24). The high value during the later daylight hours was noted for α-cells, whereas the β-cells showed maxima at noon and at midnight. Figure 25 illustrates the relationship between the nuclear size of the α- and β-cells.

The question arises whether the described variations represent inherent rhythms or are rather effects of given sleep-activity patterns and meal schedules. Most studies performed in this field were carried out with people on their normal life schedules. Recently, some results have been described suggesting that the factors associated with the patterns of sleep and nutrition somehow control the diurnal variations in glucose tolerance. Jarrett (10) cites the studies performed by Cambell in the Antarctic during midwinter when darkness was continuous. The control group

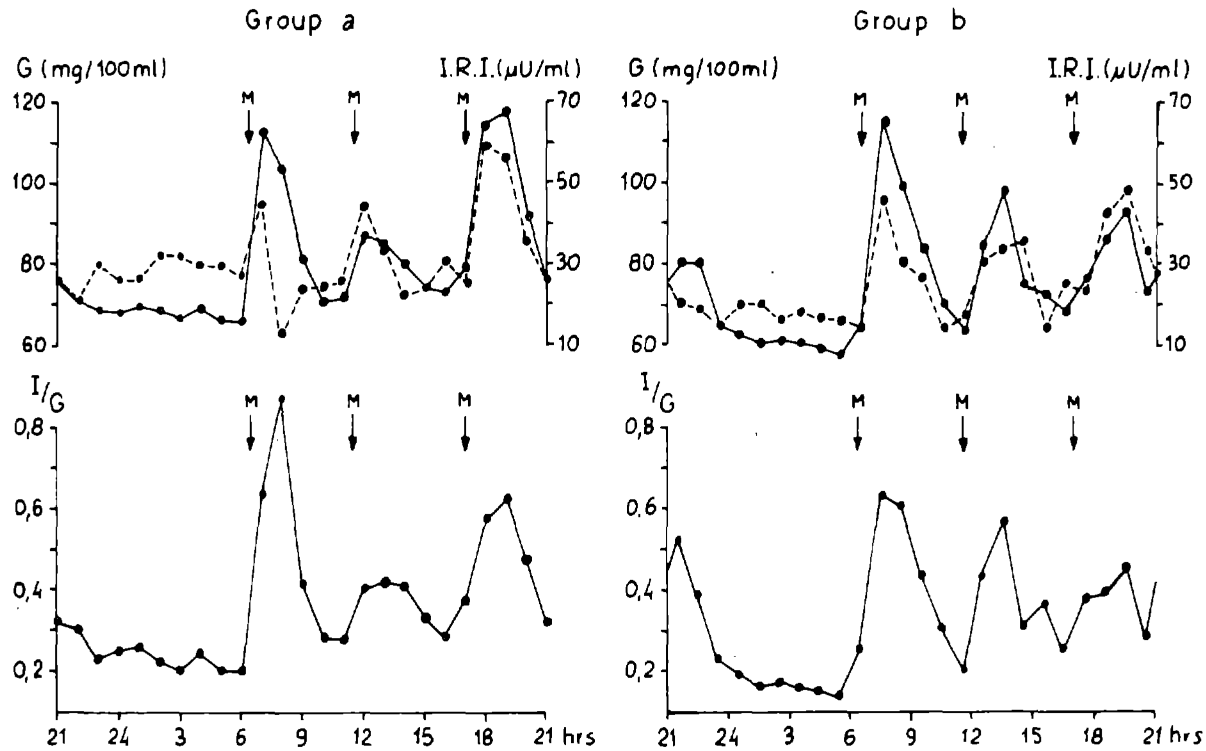


Figure 9. Circadian variations of blood sugar (---), plasma insulin (—), and the I/G ratio in seven normal subjects receiving three different meals (M) at 6:30 a.m., 11:30 a.m., and 5 p.m. Group "a" had different amounts of calorie content: 700 Cal at 6:30 a.m., 1180 Cal at 11:30 a.m., and 450 Cal at 5 p.m. Group "b" had identical calorie contents of 745 Cal (Malherbe, de Gasparo, de Hertogh, and Hoet, 1969).

of people adapted spontaneously to a 25 to 26 hour day with a reversed sleeping pattern, getting up about 5 p.m. and going to bed at about 6 a.m. A significant, but reversed, diurnal variation in glucose tolerance in comparison with the chronological expectation was observed in these people.

The changes in diurnal pattern of the life-schedule were probably the cause of the reversal of diurnal fluctuations in glucose tolerance observed by Trenchard and Jennings (21) in men after fasting. These authors examined healthy young males 22 to 24 years old in the morning (9 a.m. to 1 p.m.) and afternoon (1 p.m. to 5 p.m.), both after 4-hour and 12-hour fasting periods. In the case of 12 hours of fasting, the last meal was served at 1 a.m., instead of the normal daytime period. The existence of a relative afternoon intolerance was noted in the situation when the afternoon test was preceded by a four hour fast. However, it was interesting that an improvement of glucose tolerance in the afternoon test was observed when the test was preceded by a 12-hour fast (fig. 26).

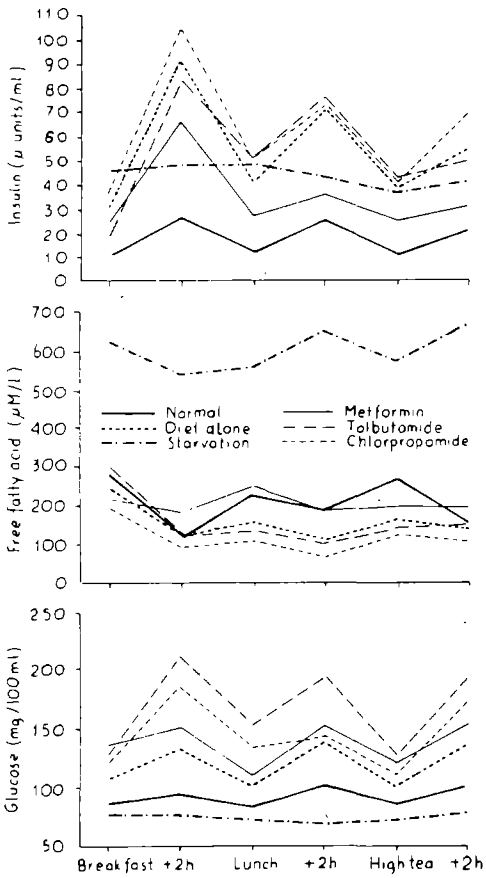


Figure 10. Mean circadian variations of glucose, free fatty acids, and insulin in the six groups (Rigas, Bittles, Hadden, and Montgomery, 1968).

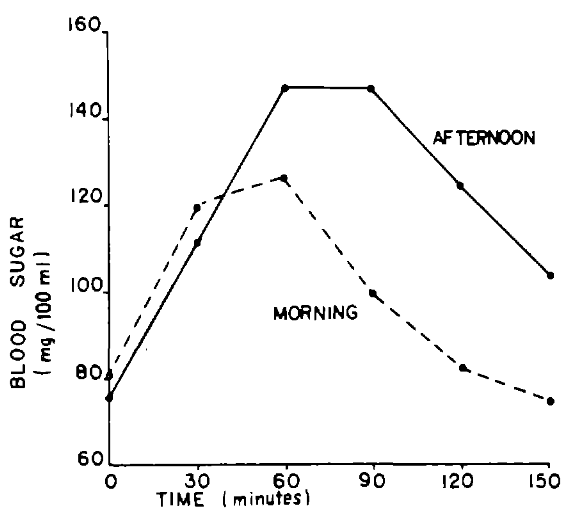


Figure 11. Mean blood sugar levels (mg/100 ml) for whole group (n = 31) in the two glucose tolerance tests (Zimmet, Wall, Rome, Stimmler, and Jarrett, 1974).

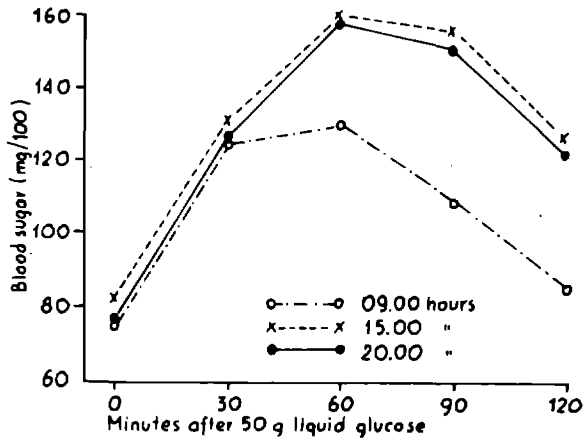


Figure 12. Mean blood sugar curves in the three glucose tolerance tests (n = 24; Jarrett, Baker, Keen, and Oakley, 1972).

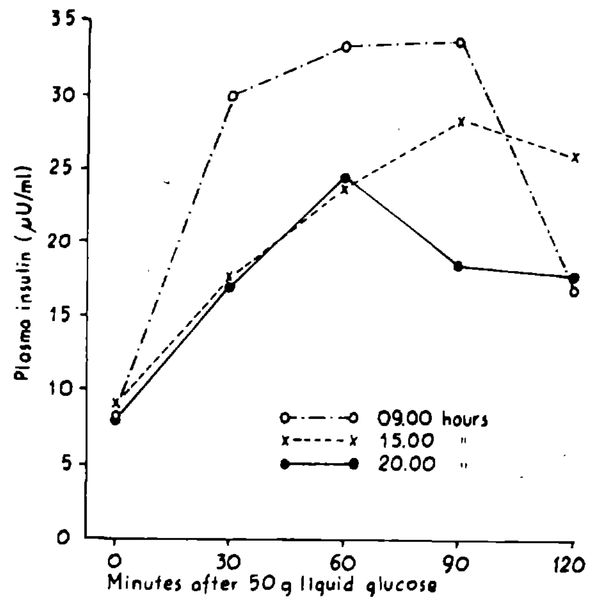


Figure 13. Mean plasma immunoreactive insulin levels during the three glucose tolerance tests (n = 24; Jarrett, Baker, Keen, and Oakley, 1972).

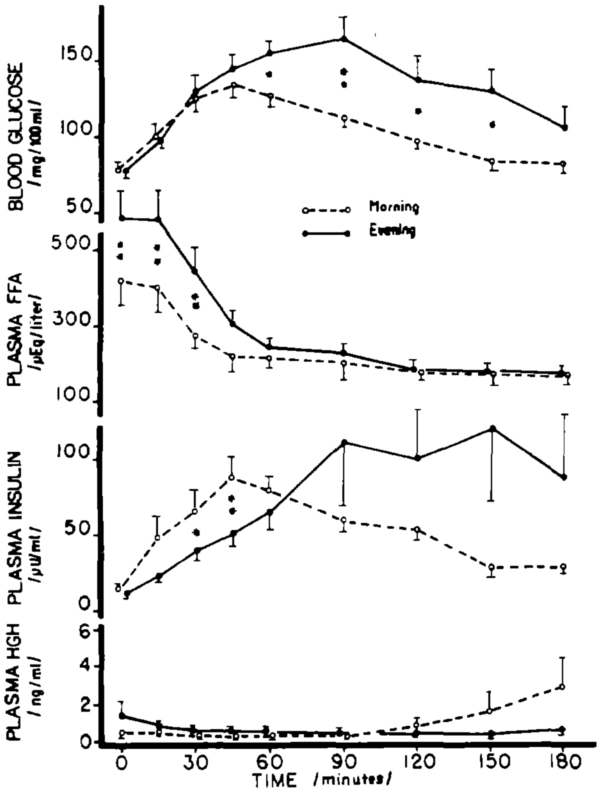


Figure 14. Blood glucose and plasma FFA insulin and HGH concentrations (mean ± SE) during oral glucose tolerance tests at 7 a.m. and 7 p.m. in eight normal subjects. Significance of the differences between the morning and evening values by paired-students' tests are indicated in this figure as follows: * = $p < 0.05$ and ** = $p < 0.01$ ($n = 8$; Carroll, and Nestel, 1973).

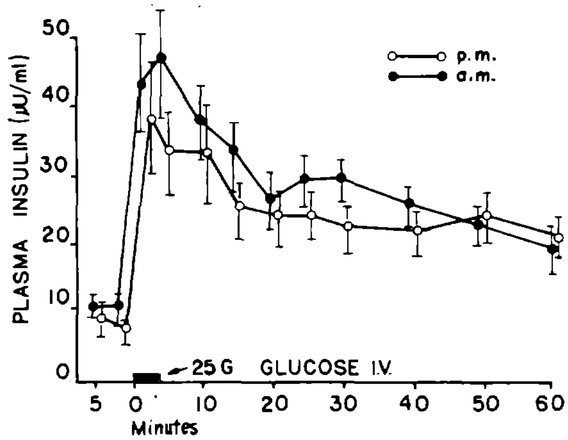


Figure 16. Plasma insulin (mean ± SE) during morning and afternoon tests (Whichelow, Sturge, Keen, Jarrett, and Stimmler, 1974).

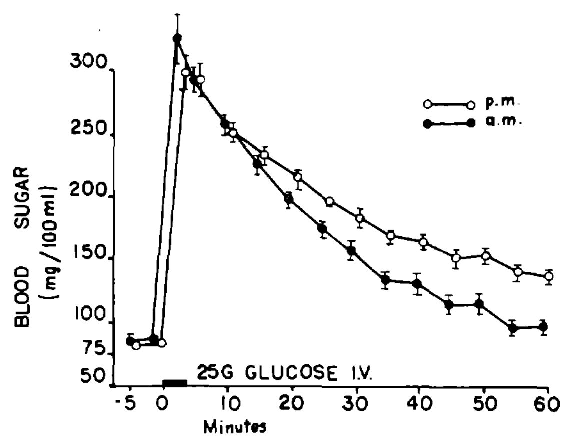


Figure 15. Blood sugar levels (mean ± SE) during morning and afternoon tests ($n = 13$; Whichelow, Sturge, Keen, Jarrett, and Stimmler, 1974).

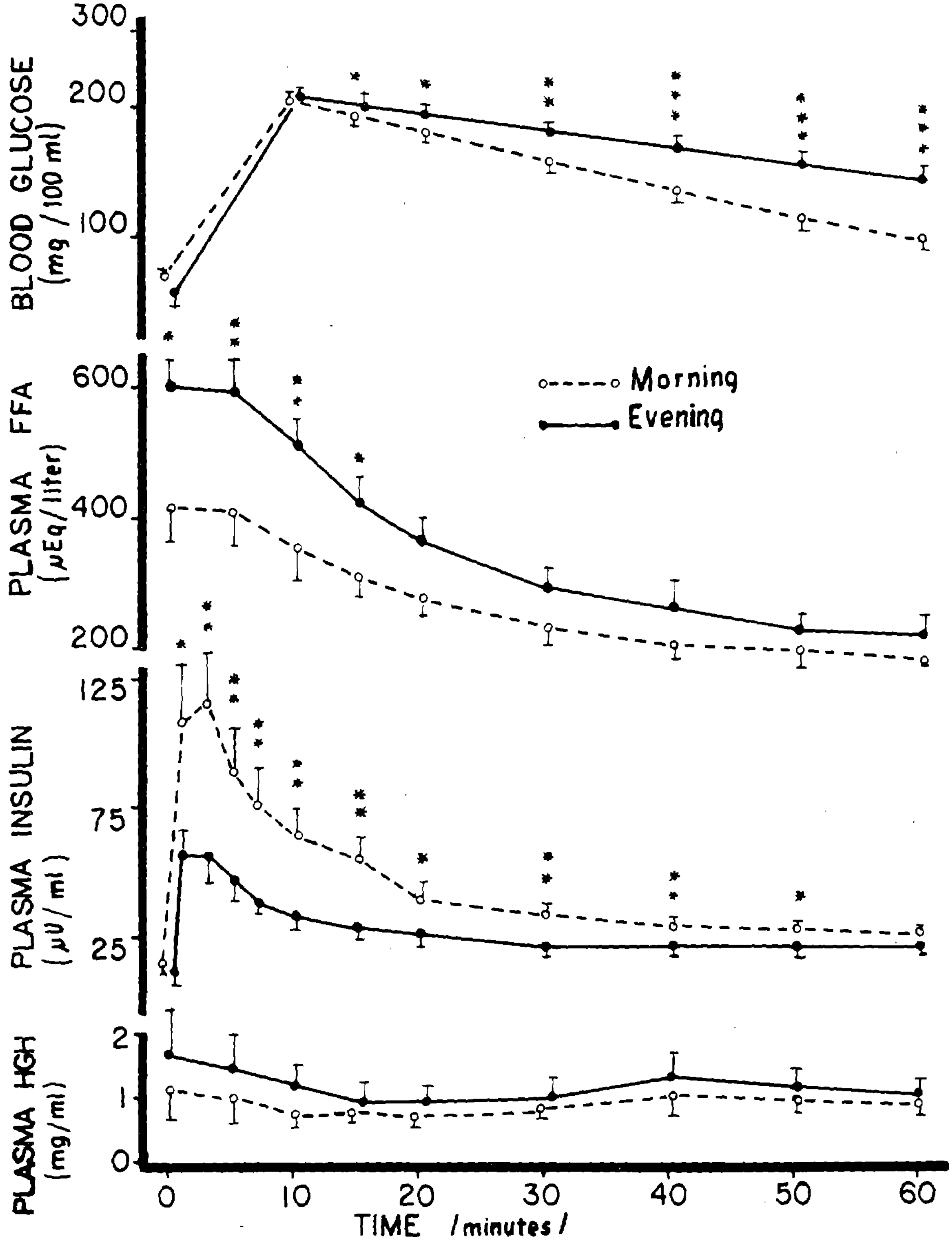


Figure 17. Blood glucose, plasma FFA, insulin, and HGH concentrations (mean ± SE) during intravenous glucose tolerance tests at 7 a.m. and 7 p.m. in 11 normal subjects (= $p<0.05$, ** = $p<0.01$, and *** = $p<0.001$; Carroll and Nestel, 1973).*

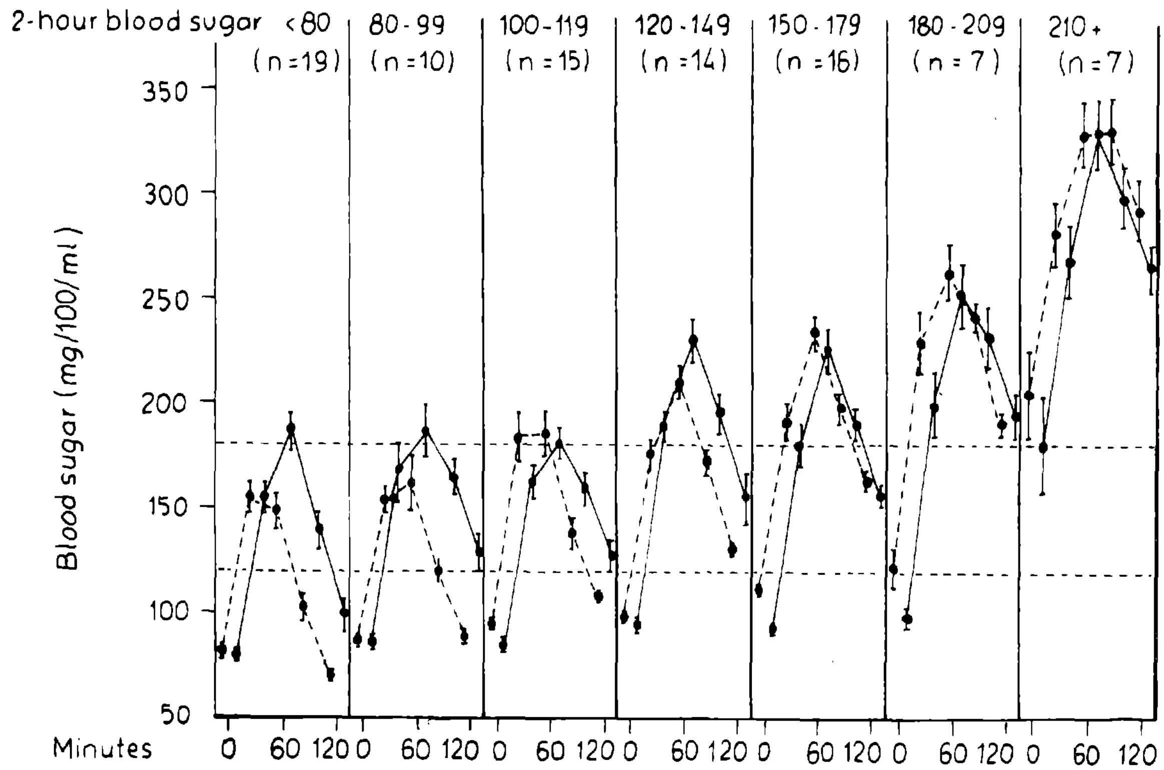


Figure 18. Mean blood sugar levels in oral glucose tolerance tests performed at 9:30 a.m. (---) and 4:30 p.m. (—), respectively. This group of male subjects is subdivided according to the level of the blood sugar two hours after the glucose load in the morning (Jarrett and Keen, 1970).

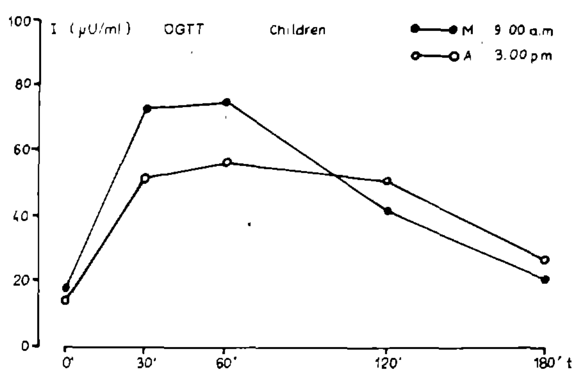


Figure 19. Insulin levels during OGTT in children (n = 20; Lestradet, Deschamps, and Giron, 1974).

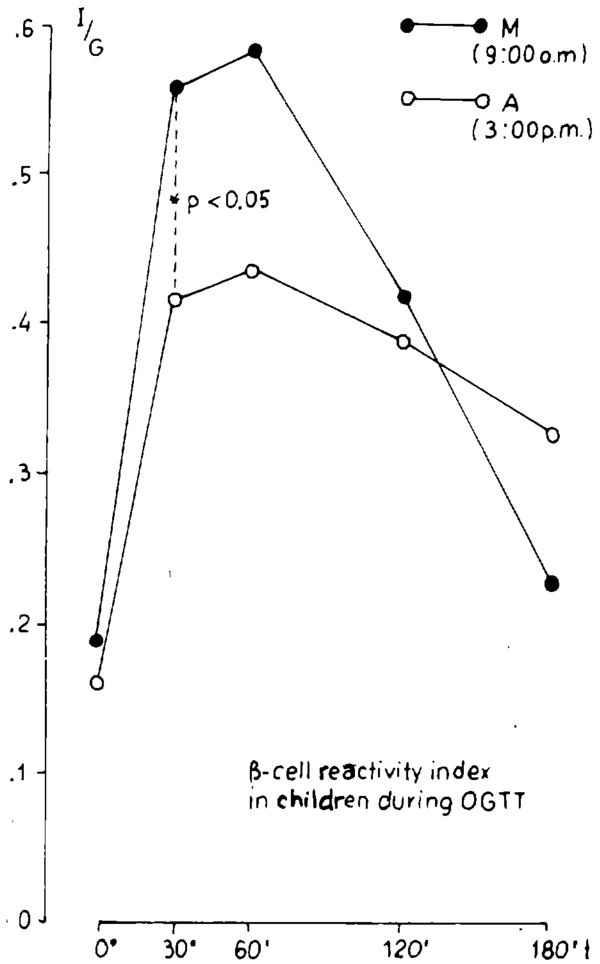


Figure 20. Insulin/glucose index during morning and afternoon OGTT in children (n = 20; Lestradet, Deschamps, and Giron, 1974).

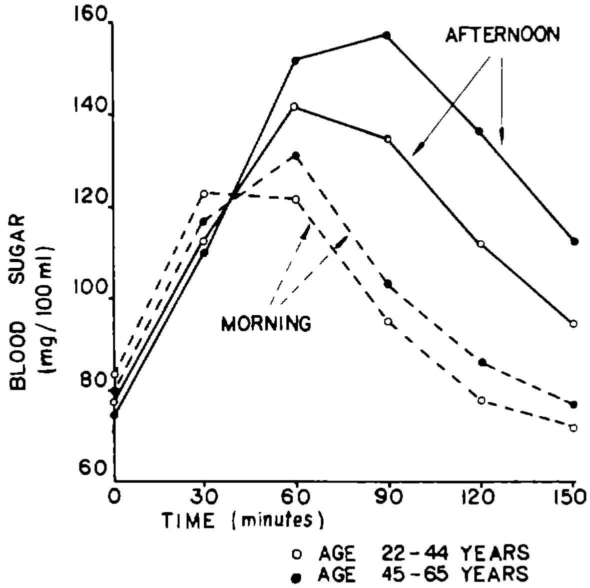


Figure 22. Mean blood sugar levels in age groups of 22 to 44 and 45 to 65 years (Zimmet, Wall, Rome, Stimmler, and Jarrett, 1974).

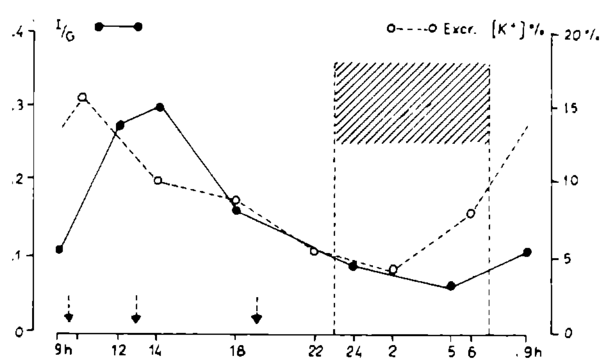


Figure 21. Circadian variation of I/G index and potassium renal excretion (Lestradet, Deschamps, and Giron, 1974).

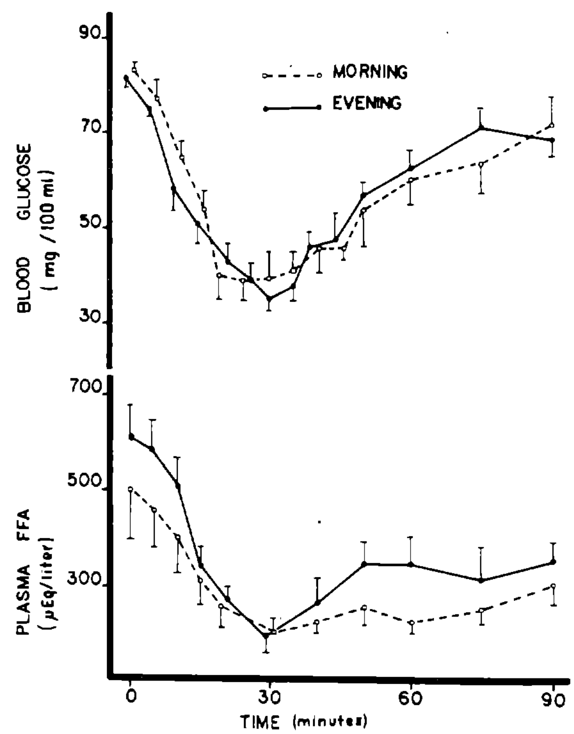


Figure 23. Blood glucose and plasma FFA concentration (mean ± SE) during insulin tolerance tests at 7 a.m. and 7 p.m. in six subjects (Carroll and Nestel, 1973).

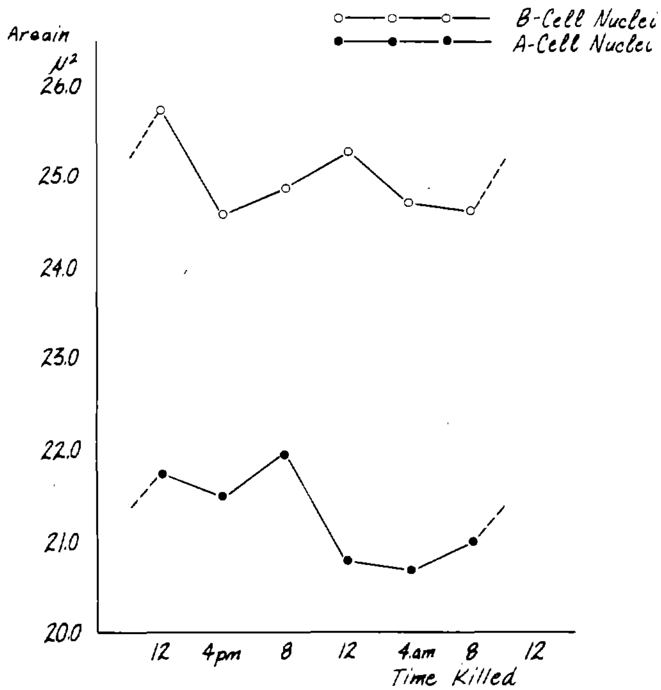


Figure 24. Diurnal changes in the size of the islet cell nuclei of normal rats (Hellman and Hellerstrom, 1959).

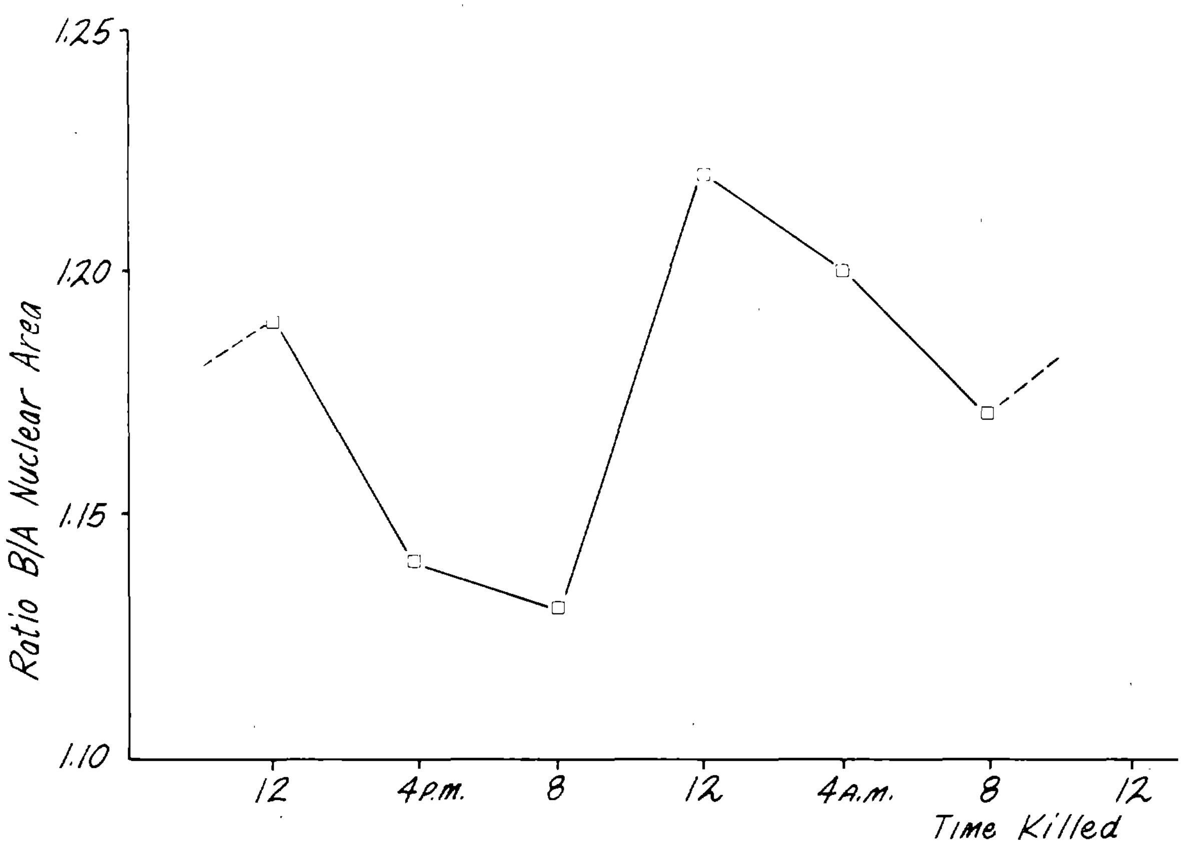


Figure 25. Diurnal changes in the ratio of β- and α-cell nuclear areas (Hellman and Hellerstrom, 1959).

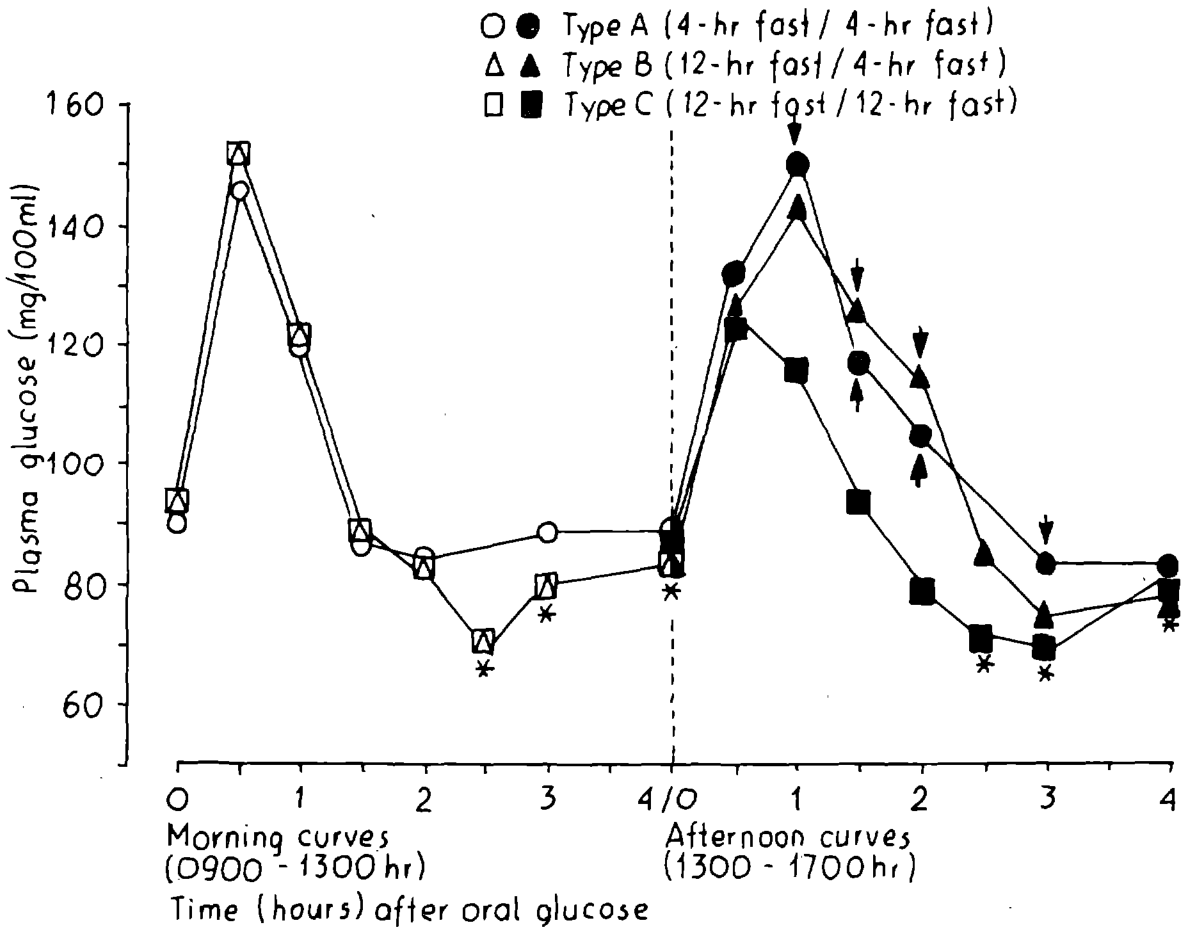


Figure 26. Glucose responses of types A, B, and C during the day. Arrows indicate type A and B values which differed significantly ($p < 0.05$) from those of type C. Symbols marked with asterisk denote values that lay significantly ($p < 0.05$) below zero time value (fasting) for that curve. There were no 2 1/2-hour values for type A (Trenchard and Jennings, 1974).

CHAPTER VIII

CIRCADIAN VARIATIONS IN PHYSIOLOGICAL REACTIONS TO PHYSICAL WORK

It is important, for practical reasons, to know whether the physiological reactions to physical work are independent of the time of day the work is performed. Some information has been presented in Chapter II. The results of recent investigations in which the physical load did not exceed the level commonly accepted for occupational work are presented here.

General Procedure

The subjects (healthy young students, 23 women and 20 men), leading a normal life-schedule with day activity and night sleep, were examined on the ergometer at different times of the day. The external load was the same for a given subject in all experiments and it was chosen during preliminary experiments to be about 30 percent of each individual's maximal aerobic capacity ($\dot{V}_{O_2}$ max). The people were examined during short experiments with work periods of 10 minutes; during intermediate work periods of 30 and 70 minutes for women and men, respectively, and during long work periods of 8 hours. The 8 hour work periods were interrupted every 30 and 70 minutes with 25 and 35 minutes of rest for women and men, respectively. Thus, there were nine or five work cycles during each 8-hour session. Each experiment was repeated at different times of the day; once in the morning at 8 a.m., once in the afternoon at 4 p.m., and once at midnight. Thus, in the case of the long work sessions, the subjects worked from 8 a.m. to 4 p.m. (morning session), from 4 p.m. to midnight (afternoon session), and from midnight to 8 a.m. (night session). The experimental sessions were performed in a random order with only one session being carried out on any experimental day.

Results

Only slight differences in the physiological responses were observed during the short and the intermediate work period experiments. The differences were mainly in the values of net pulse rate and net cardiac work cost (i.e., the values above resting level). Thus, during the short work, the net pulse rate was significantly lower when the work was performed at 8 a.m. in comparison to the rates taken at 4 p.m. ($p = 0.039$) and at midnight ($p = 0.001$; $n = 23$). At the same time (fig. 27), there were no significant differences in absolute values of these parameters and often, even lower values were noted at night because of the lower resting levels at night.

Similar results were obtained when the subjects were examined during the intermediate work periods. It was shown that net cardiac work cost (fig. 28), was higher in the afternoon (at 4:30 p.m.) and at night (at 12:30 a.m.) than in the morning (at 8:30 a.m.) ($p = 0.039$ and $p = 0.029$, respectively; $n = 23$). Thus, it can be concluded that the evaluation of physiological cost of physical work should not be based on absolute values when the measurements taken in different time of day are compared, but rather net values should be used.

The differences in physiological parameters, which were related to the time of day, were greater when the measurements were taken during prolonged work. These differences were present for the net values of pulse rate and cardiac work cost; the absolute values sometimes revealed similar differences. It has been shown that both parameters increased during successive work cycles through the 8-hour session, but especially when the work started at midnight (figs. 29, 30, 31). The differences between the measurements

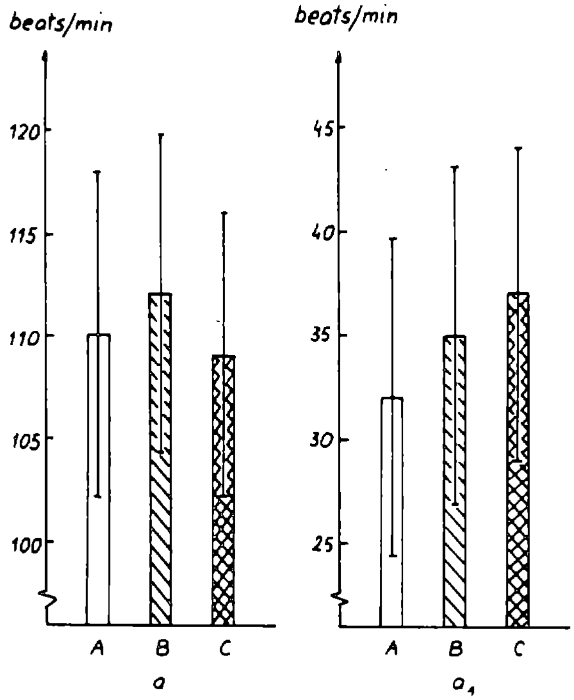


Figure 27. Pulse rate (a) and net pulse rate (a_1); the measurements taken between 5 and 10 minutes of cycling at 8 a.m. (A), 4 p.m. (B), and at midnight (C) in women (n= 23).

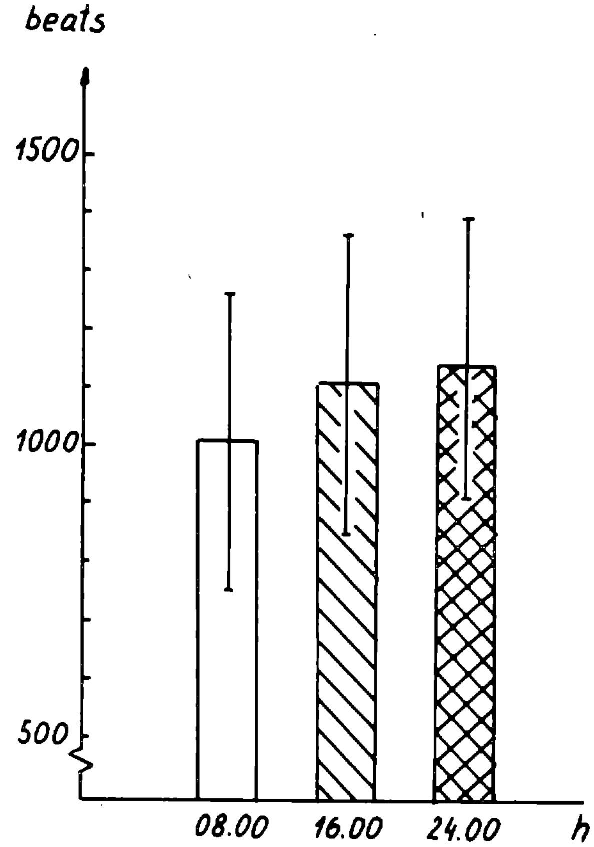


Figure 28. Net cardiac work cost during 30 minutes of cycling in different times of day for women. The work started at 8 a.m., 4 p.m., and at midnight (n = 23).

for comparable work cycles of different sessions are seen on figures 32,33,34, and 35. The higher values were more frequently observed during night and afternoon sessions than during morning ones. It was characteristic that at the end of 8 hours of night work, at 8 a.m., net pulse rates (fig. 33) and net cardiac work cost (fig. 35) were significantly higher than they were at the end of 8 hours of day work at 4 p.m. ($p = 0.005$ and $p = 0.003$, respectively; $n = 23$). Also after 3-hours work (2nd work cycle), net cardiac work cost (fig. 34) was significantly lower in the morning (about 10:30 a.m.) than after the same period of work performed in the afternoon (about 6:30 p.m.; $p = 0.012$) and at night (about 2:30 a.m.; $p = 0.028$).

There were also similar differences in oxygen consumption and energy expenditure. Generally, the highest values were noted at night or in the evening compared with similar cycles of the morning session. Thus, after 4 hours of work, oxygen uptake was higher at night (about 4:30 a.m.) and in the evening (about 8:30 p.m.) than after the same work period performed at about noon ($p = 0.034$ and $p = 0.024$, respectively; $n = 20$).

It should be mentioned that the respiratory quotient (RQ) decreased slightly in the later part of the day. Thus, the values noted at about midnight were lower than those at 4:30 p.m. ($p = 0.013$; $n = 23$). During work of 30 minutes, the RQ was lower at midnight than in the afternoon ($p = 0.005$). Similarly, after 8 hours of work (fig. 36) the RQ was lower at midnight (the end of afternoon session) than at the end of morning session at 4 p.m. ($p = 0.037$; $n = 23$).

Thus, in the experiments presented above, the physiological cost of physical work was slightly higher at night, inspite of the fact that the external load did not exceed the load commonly accepted for daily occupational work, i.e., 30 percent of individual $\dot{V}_{O_2}$ max. It resulted in a higher night time net heart rate and net cardiac work cost. These differences were not revealed when the absolute values of heart rate and cardiac work cost were used as indicators because of lower resting level of these parameters at night. Thus, the absolute values should not be used in assessing circadian variations in the physiological cost of physical work. Net cardiac work cost seems to be

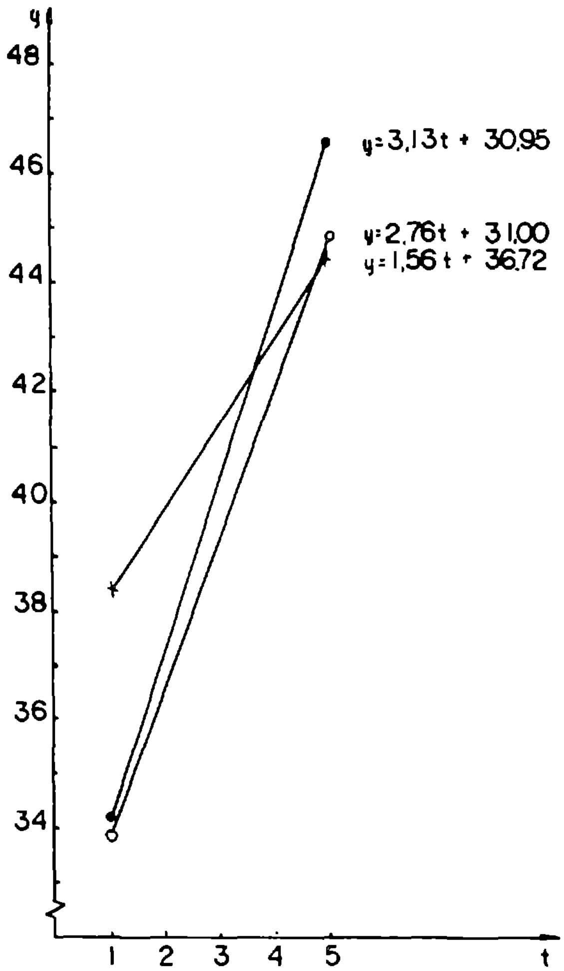


Figure 29. Regression lines representing the rise of net pulse rate during successive work cycles (t) of three experimental sessions (men, n = 20): (o—o) morning, 8 a.m. to 4 p.m.; (x—x) afternoon, 4 p.m. to midnight; and (o—o) night, midnight to 8 a.m.

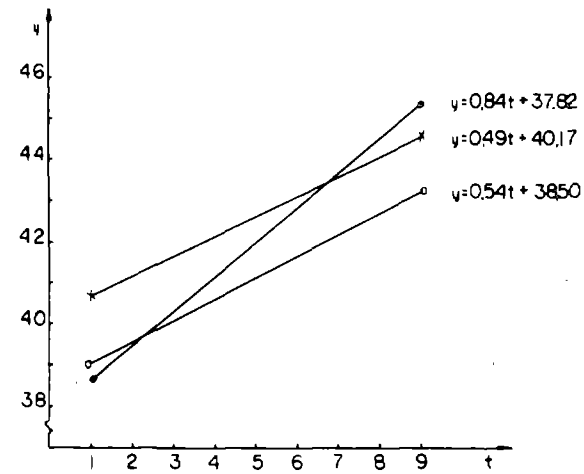


Figure 30. Regression lines representing the rise of net pulse rate during successive work cycles (t) of three experimental sessions (women, n = 23): (o—o) morning, 8 a.m. to 4 p.m.; (x—x) afternoon, 4 p.m. to midnight; and night (o—o), midnight to 8 a.m.

the best indicator that might be used while comparing the physiological strain of physical work performed at different times of the day.

The differences which have been reported for the respiratory quotient were probably connected with circadian variations in energy metabolism as a consequence of the changes in the interrelationship between the carbohydrates and lipids which are utilized under the conditions of physical work.

The investigations were supported by Polish-American agreement 05-015-2 and 05-015-3.

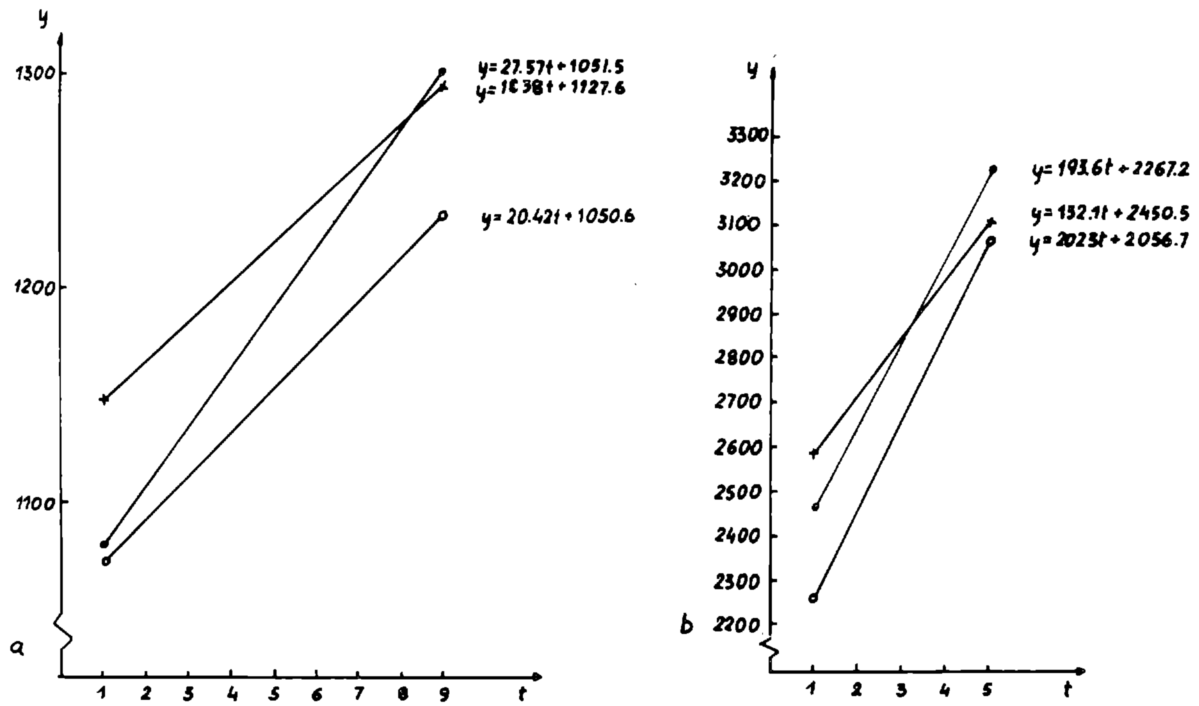


Figure 31. Regression lines representing the rise of net cardiac work cost during successive work cycles (t) of three experimental sessions: (o—o) morning, 8 a.m. to 4 p.m.; (x—x) afternoon, 4 p.m. to midnight; and (o—o) night, midnight to 8 a.m. (women "a", n = 23; men "b", n = 20).

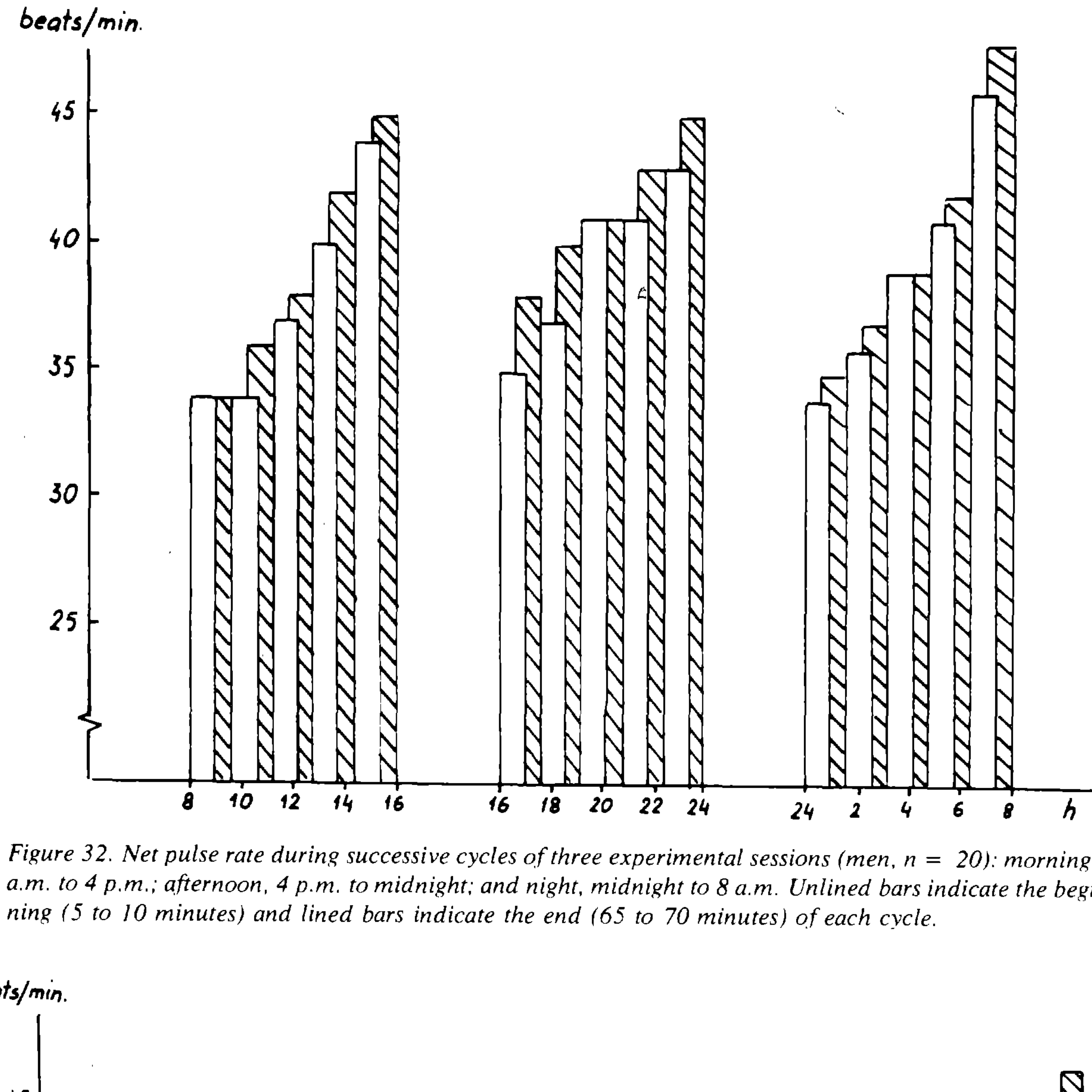


Figure 32. Net pulse rate during successive cycles of three experimental sessions (men, n = 20): morning, 8 a.m. to 4 p.m.; afternoon, 4 p.m. to midnight; and night, midnight to 8 a.m. Unlined bars indicate the beginning (5 to 10 minutes) and lined bars indicate the end (65 to 70 minutes) of each cycle.

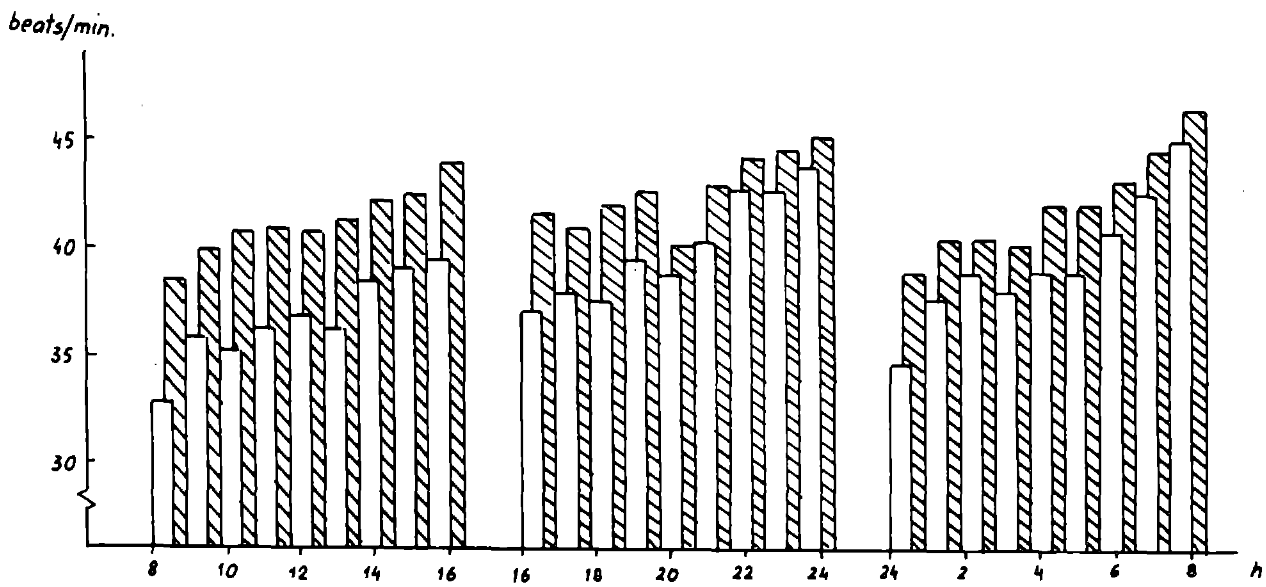


Figure 33. Net pulse rate during successive cycles of three experimental sessions (women, n = 23): morning, 8 a.m. to 4 p.m.; afternoon, 4 p.m. to midnight; and night, midnight to 8 a.m. Unlined bars indicate the beginning (5 to 10 minutes) and lined bars indicate the end (65 to 70 minutes) of each cycle.

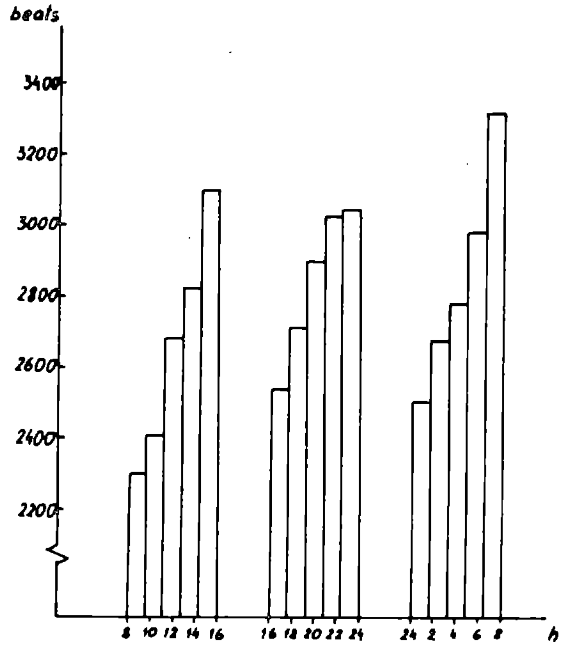


Figure 34. Net cardiac work cost during successive work cycles of three experimental sessions (men, n = 20): morning, 8 a.m. to 4 p.m.; afternoon, 4 p.m. to midnight; midnight to 8 a.m.

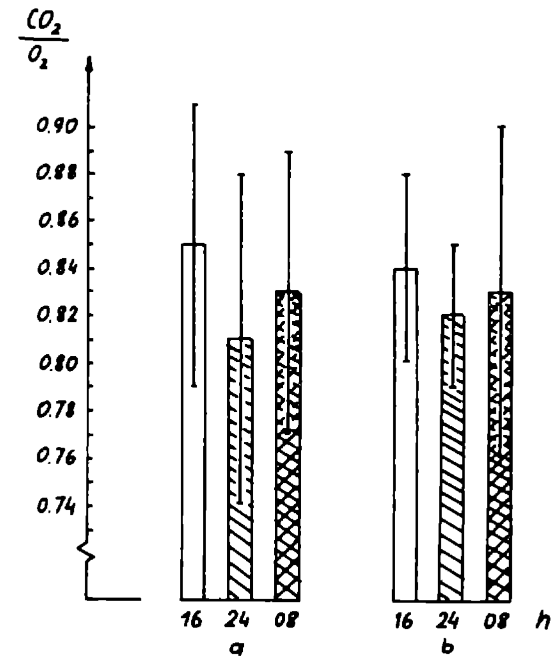


Figure 36. Respiratory quotient estimated at the end of three experimental sessions (i.e., after 8-hour work periods): at 4 p.m. for the morning session; (unlined bars) at midnight for the afternoon session (lined bars); and at 8 a.m. for the night session (cross-lined bars). ("a" women, n = 23; men "b", n = 20.)

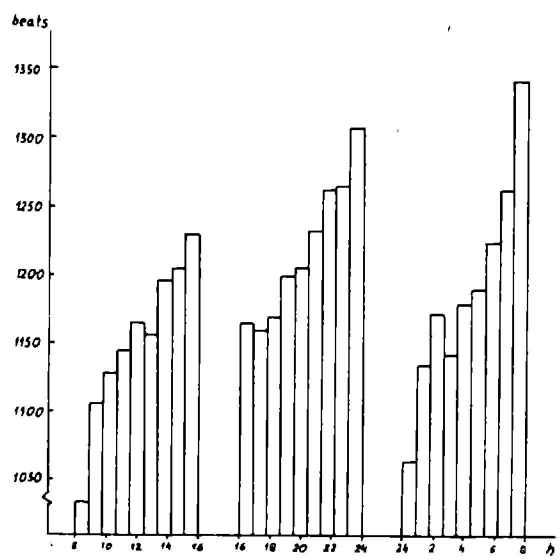


Figure 35. Net cardiac work cost (sum of heart beats above resting level) during successive work cycles of three experimental sessions (women, n = 23): morning, 8 a.m. to 4 p.m.; afternoon, 4 p.m. to midnight; and night, midnight to 8 a.m.

CHAPTER IX

THE INFLUENCE OF PHYSICAL EXERCISE ON CIRCADIAN VARIATIONS IN 17-KS URINARY EXCRETION

There are several factors which can change the course of biological circadian rhythms; e.g., changes in the light/dark regimen, in meal schedule, or in ambient temperature. The role of synchronizers in timing the phases of biological rhythms has been treated in Chapter I. In the investigations presented below, the influence of physical effort performed at different times of the day on circadian fluctuation in 17-KS urinary excretion was studied.

Procedure

Series A The levels of urinary 17-KS excretion were measured in healthy people (13 women and 10 men, age 19 to 27 years) working on the ergometer. The work was performed for 8 hours and the urine was collected every 4 hours over 24-hour periods, starting with the beginning of the work and ending 16 hours after finishing the work. The physical load was chosen individually to be about 30 percent of $\dot{V}_{O2}$ max, as a borderline load commonly accepted for daily occupational work. Each subject worked at different times of the day: 8 a.m. to 4 p.m. (morning-session), 4 p.m. to midnight (afternoon session), and midnight to 8 a.m. (night session). The work was interrupted every 30 to 70 minutes for 25 and 35 minutes of rest for women and men, respectively. The sessions were performed in a different sequence for each subject. Each session was carried out on a separate experimental day with about a week between successive sessions.*

The subject led a normal life with day activity and night sleep, except for the night experiments before which they were asked to sleep in the preceding afternoon.

Series B As in Series A, the levels of urinary 17-KS excretion were estimated in the same individuals, but during their normal life and with no physical exercise. They participated in normal student activities during daytime hours and slept at night. The samples of urine were collected continuously every 4 hours as in Series A. Each subject was examined on 3 separate days. Thus, a comparison could be made between the levels of 17-KS recorded in samples collected in Series A and with those recorded at the same hours in Series B.

Results

Clear circadian variations in urinary 17-KS excretion were shown in Series B when the subjects were examined during their normal life schedule. The maximum and minimum occurred at about 8 p.m. and 4 a.m., respectively, for men (fig. 37) and at about noon and midnight, respectively, for women (fig. 38). The amplitude of circadian variations was higher for the men ($p<0.001$), than for the women.

Physical effort (Series A) caused an elevation of urinary 17-KS excretion. Thus, the levels noted during work were higher than those noted during the normal life routine. The work effect was apparent in particular for the samples collected at noon in the women ($p<0.001$) and at 8 p.m. and 4 a.m. in the men ($p= 0.034$ and $p= 0.044$, respectively).

It was characteristic that after finishing work, the concentration of 17-KS in urine decreased rapidly to levels which were sometimes lower than those noted at the same hours in Series B.

* In the case of women, the experiments were stopped for a period of about 10 days including the menses.

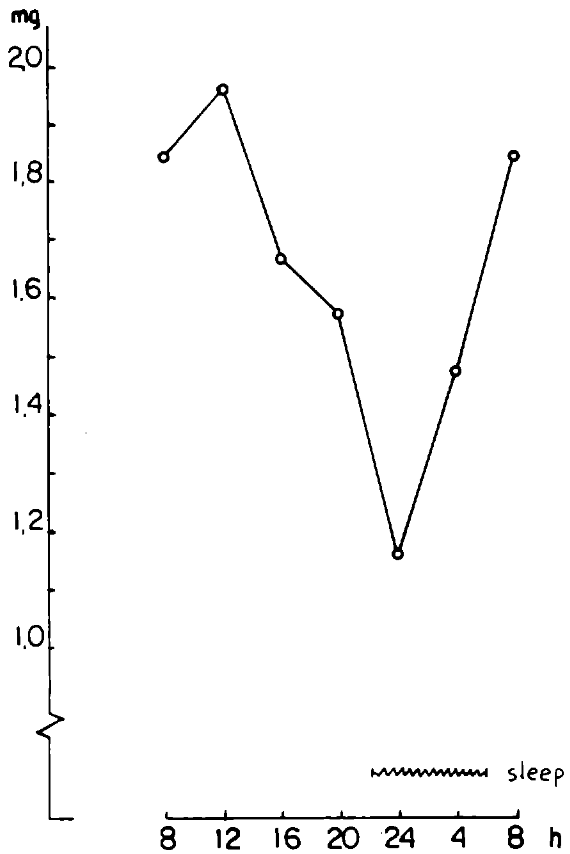


Figure 37. 17-KS urinary excretion estimated every 4 hours during normal life schedule (men, n = 10).

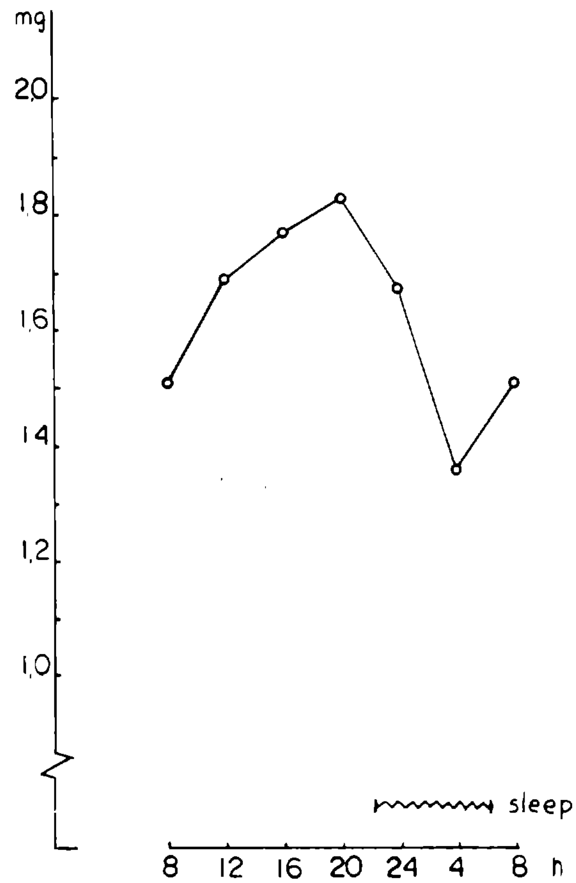


Figure 38. 17-KS urinary excretion estimated every 4 hours during normal life schedule (women, n = 13).

Such a sharp fall was noted at midnight if the work was done between 8 a.m. and 4 p.m., and at 4 a.m. if the work was performed between 4 p.m. and midnight for both the women and the men. Thus, in the case of the morning session the levels of 17-KS were highest in samples collected 4 hours after work and lowest in samples collected 8 hours after the end of the work ($p<0.001$ and $p=0.002$, for women and men, respectively). Similarly, during the afternoon session the levels were highest after 4 hours of work but lowest after 4 hours of recovery ($p=0.007$ and $p=0.04$, for women and men, respectively). On the other hand, when the work was done at night (midnight to 8 a.m.) the highest levels were mostly noted after 8 hours of work and the fall in level continued until the next night.

However, the circadian fluctuations were still sustained when the physical work was performed in day hours, i.e., during morning and afternoon sessions (figs. 39, 40, 41, 42) for both women and men. It was also sustained when the work was done at night (night session) but only in the men (fig. 43). In the women (fig. 44), the circadian rhythm was completely abolished when the subjects work from midnight to 8 a.m.

Therefore, it can be concluded that the influence of the physical effort upon circadian fluctuations of urinary 17-KS excretion depended on the time of day when the work was performed. This influence was marked, in particular, in the case of the women when they worked at night.

The investigations were supported by Polish-American agreement; Contract Nos. 05-015-2 and 05-015-3.

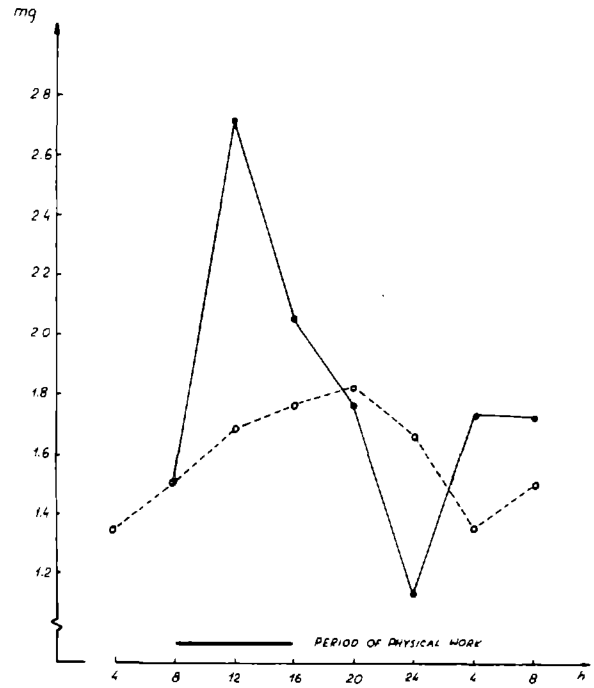


Figure 39. 17-KS urinary excretion: Series A (solid line), the work performed from 8 a.m. to 4 p.m.; Series B (broken line), normal life schedule (women, n = 13).

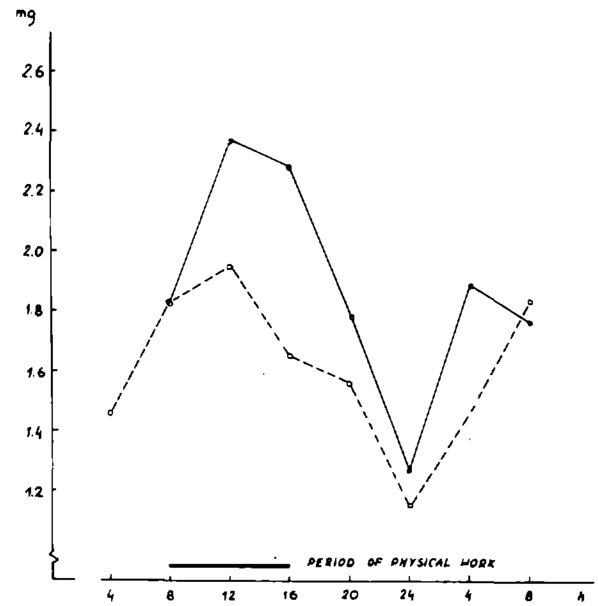


Figure 41. 17-KS urinary excretion: Series A (solid line), the work performed from 8 a.m. to 4 p.m.; Series B (broken line), normal life schedule (men, n = 10).

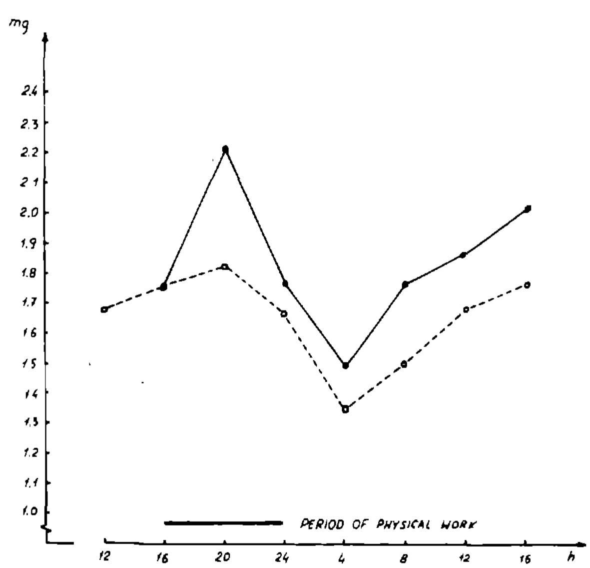


Figure 40. 17-KS urinary excretion: Series A (solid line), the work performed from 4 p.m. to midnight; Series B (broken line), normal life schedule (women, n = 13).

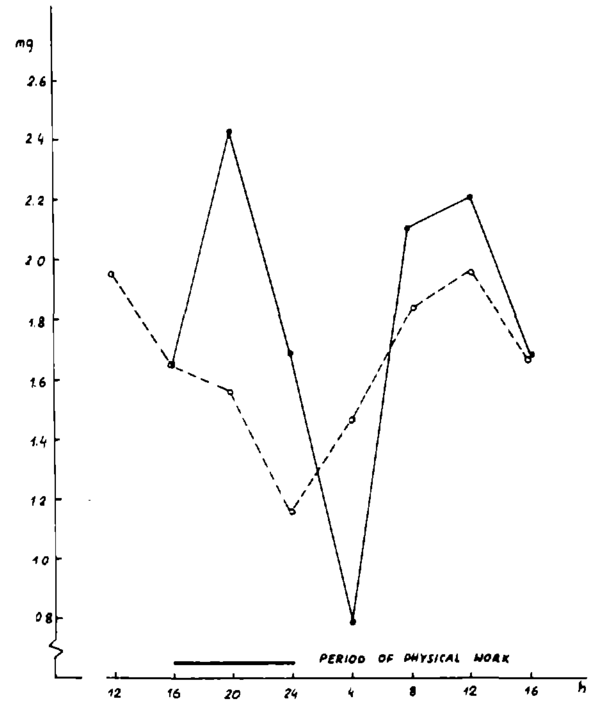


Figure 42. 17-KS urinary excretion: Series A (solid line), the work performed from 4 p.m. to midnight; Series B (broken line), normal life schedule (men, n = 10).

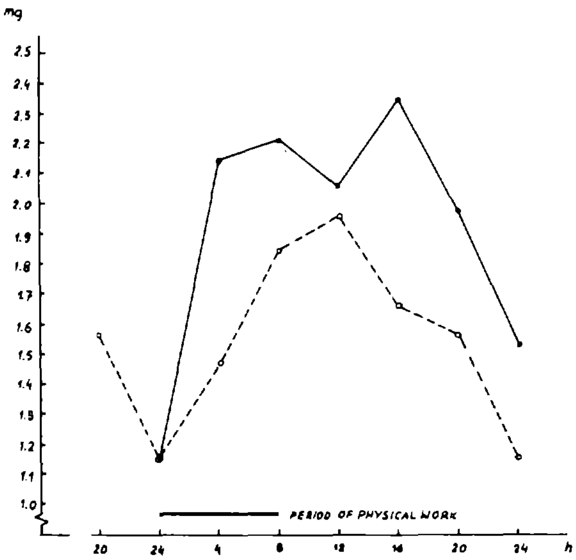


Figure 43. 17-KS urinary excretion: Series A (solid line), the work performed from midnight to 8 a.m.; Series B (broken line), normal life schedule (men, n = 10).

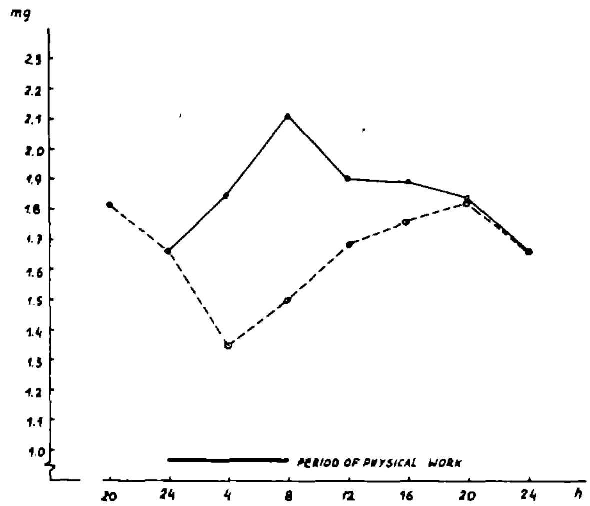


Figure 44. 17-KS urinary excretion: Series A (solid line), the work performed from midnight to 8 a.m.; Series B (broken line), normal life schedule (women, n = 13).

REFERENCES

1. Baker, I. A., and R. J. Jarrett (1972): *Diurnal variation in the blood-sugar and plasma-insulin response to tolbutamide.* **Lancet** 4:945.
2. Barter, P. J., K. F. Carroll, and P. J. Nestel (1971): *Diurnal fluctuations in triglyceride, free fatty acids, and insulin during sucrose consumption and insulin infusion in man.* **J. Clin. Invest.** 50:583.
3. Bowen, A. J., and R. L. Reeves (1967): *Diurnal variation in glucose tolerance* **Arch. Intern. Med.** 119:261.
4. Carroll, K. F., and P. J. Nestel (1973): *Diurnal variation in glucose tolerance and in insulin secretion in man.* **Diabetes** 22:333.
5. Faiman, C., and J. A. Moorhouse (1967): *Diurnal variation in the levels of glucose and related substances in healthy and diabetic subjects during starvation.* **Clinical Science** 32:111.
6. Freinkel, N., M. Mager, and L. Vinnick (1968): *Cyclicity in the interrelationships between plasma insulin and glucose during starvation in normal young men* **J. Lab. Clin. Med.** 71:171.
7. Gibson, T., and R. J. Jarrett (1972): *Diurnal variation in insulin sensitivity.* **Lancet** 2:947.
8. Hansen, A. P., and K. Johansen (1970): *Diurnal patterns of blood glucose, serum free fatty acids, insulin, glucagon, and growth hormone in normals and juvenile diabetics.* **Diabetologia** 6:27.
9. Hellman, B., and C. Hellerstrom (1959): *Diurnal changes in the function of the pancreatic islets of rats as indicated by nuclear size in the islet cells.* **Acta Endocrinologica** 31:267.
10. Jarrett, R. J. (1974): *Diurnal variation in glucose tolerance; associated changes in plasma insulin, growth hormone, and non-esterified fatty acids and insulin sensitivity.* Chronobiological Aspects of Endocrinology, Symposium, Capri, 229.
11. Jarrett, R. J., and H. Keen (1969): *Diurnal variation of oral glucose tolerance: a possible pointer to the evaluation of diabetes mellitus* **Brit. Med. J.** 2:341.
12. Jarrett, R. J., and H. Keen (1970): *Further observations on the diurnal variation in oral glucose tolerance* **Brit. Med. J.** 4:334.
13. Jarrett, R. J., I. A. Baker, H. Keen, and N. W. Oakley (1972): *Diurnal variation in oral glucose tolerance: blood sugar and plasma insulin levels morning, afternoon, and evening.* **Brit. Med. J.** 1:199.
14. Lambert, A. E., and J. J. Hoet (1965): *Diurnal pattern of plasma insulin concentration in the human.* **Diabetologia** 2:69.
15. Lestradet, H., I. Deschamps, and B. Giron (1974): *Diurnal variations of insulin in normal children.* Chronobiological Aspects of Endocrinology, Symposium, Capri, 239.
16. Malherbe, C., M. de Gasparo, R. de Hertogh, and J. J. Hoet (1969): *Circadian variations of blood sugar and plasma insulin levels in man.* **Diabetologia** 5:397.
17. Oakley, N. W., D. Monier, and V. Wynn (1973): *Diurnal variation in oral glucose tolerance: insulin and growth hormone changes with special reference to women taking oral contraceptives.* **Diabetologia** 9:235.
18. Quabbe, H. J., E. Schilling, and H. Helge (1966): *Pattern of growth hormone secretion during a 23-hour fast in normal adults.* **J. Clin. Endocr.** 26:1173.
19. Rigas, A. N., A. H. Bittles, D. R. Hadden, and D. A. D. Montgomery (1968): *Circadian variation of glucose, insulin, and free fatty acids during long-term use of oral hypoglycaemic agents in diabetes mellitus.* **Brit. Med. J.** 4:25.
20. Takahashi, Y., D. M. Kipnis, and W. H. Daughaday (1968): *Growth hormone secretion during sleep.* **J. Clin. Invest.** 47:2079.

21. Trenchard, P. M., and R. D. Jennings (1974): *Diurnal variation in glucose tolerance and its reversal by lengthened fasting.* **Brit. Med. J.** 2:640.
22. Whichelow, M. J., R. A. Sturge, H. Keen, R. J. Jarrett, L. Stimmler, and S. Grainger (1974): *Diurnal variation in response to intravenous glucose.* **Brit. Med. J.** 1:488.
23. Zimmet, P.Z., J. R. Wall, R. Rome, L. Stimmler, and R. J. Jarrett (1974): *Diurnal variation in glucose tolerance: associated changes in plasma insulin, growth hormone, and non-esterified fatty acids.* **Brit. Med. J.** 1:485.

☆ U.S GOVERNMENT PRINTING OFFICE: 1978— 757-141/6790