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Title: The Circadian Tide of Muman Physiological Functions in Mealth and Disease

/Sutochnyy rith fiziologicheskikh uzdorovogo i bol'nozo-chelovaka/

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This monograph presents a large collection of facts derived from investigations of the activity of physiological systems (central nervous system, digestive apparatus, cardio-vascular, and basal metabolism) at night, especially in sleep. The authors found that many changes have a more expressed pathological trend at night. This finding enabled them to devise many practical suggestions **en** how to exploit the circadian fluctuations of physiological functions for the diagnosis of ailments, how to administer drugs **the most** efficiently and how to provide food to night-workers.

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The book is meant for specialists in internal medicine.

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#### INTRODUCTION

Russian physiology and medicine, inspired by materialistic ideas of I. M. SECHEMOV, S. P. BOTKIN, I. P. PAVLOV, N. YE. VVEDENSKY, are particularly characterized by their admission of a close interrelation of the organism with the external environment. "Without an external environment that supports its existence, an organism is unlikely..."---indicated the great Russian physiologist, I. M. SECHEMOV.

By matching the rhythmic changes of Nature's phenomena, in the organism of man and animals physiological functions assumed a definitely rythmic shape. External environmental changes inevitably are reflected on physiological reactions of the organism, by conditioning a state of its equilibrium with the environment, which agrees with the doctrine of I. P. PAVLOV on the close interrelation, on the unity of the organism and its external environment. The routine circadian changes of the environment which have been returning for thousands of years as alternation of day and night create in the organism a permanent system of sequential changes in the functional state of physiological system. Diurnal fluctuations are detected in the activity of the higher departments of the central nervous system, in hemodynamics, in muscle strength and working capacity, in the activity of the digestive apparatus, and in other manifestations of vital activity.

An essential property of the diurnal routine is that the subsequent change in physiological reactions characteristic for it is still maintained for a long time even when the factors which cause the formation of routine are removed. This brings up the thought that the basis of the physiological mechanisms in the diurnal routine is the formation of reactions conditioned to time.

The circadian fluctuation of physiological functions is the most clearly shown at their study at night, especially in sleep, in comparison with the period of daytime wakefulness. But meanwhile the question of the activity of the organism at night, especially in sleep, has almost slipped out from the field of vision of research workers.

In 1954, a chrestomathic collection was published under the title "The Sleep Problem" which included the most important Russian experimental and clinical investigations conducted during the past fifty years. As the editors remarked, at that time there was "only one work, devoted to the description of changes in the physiological functions of the sleeping man, which reflects the insufficient attention paid to the indicated problem. However, the importance of physiological examinations of the functions of different organs and systems exactly in the sleeping human organism hardly needs any kind of demonstration."

The sleep problem is closely connected with the problem of inhibition. According to modern ideas, for the development of many internal ailments (hypertension, peptic ulcer, and so on) the basis is, first of all, a weakening of the inhibitory influence of the cerebral cortex upon subcortical centers. For this reason, a study of the inhibitory function of the cerebral cortex in the clinic of internal diseases has both a theoretical and a great practical importance, in particular for the elaboration of pathogenetic therapeutic methods.

For the extent of a vast historical period, active human occupation took place invariably in daytime hours, while the period of rest was ordinarily tied to nighttime. However, with the industrial development, with the organization of numerous jobs at the factory and with the need for performing them at different times of the 24-hour day, the problem of studying the characteristics of organismic function at night ceased to be merely a theoretical question, and it required State importance.

Observations show that living processes run at a higher physiological level in daytime than at night. In nighttime, the function of the circulatory system gets weaker, the metabolic processes slow down, the reflex activities of the organism diminish. From this point of view, in nighttime, an activity is "physiologically not supported with sufficient strength" (N. I. VINOGRADOV, 1958).

According to the investigations of a number of authors, in nighttime, the productivity of labor diminishes, the accuracy of carrying out individual productive operations decreases, the reject increases.

N. I. VINCGRADOV (1958) points out that, according to the findings of the Leningrad Institute for Labor Protection, at night work, the reject increases by 20%-60%, while according to the data of the Swedish scientists BIERNAR, HOLM and SVENSEN who examined the work of 175,000 workers in gas enterprises, the number of failing and erroneous actions of workers increases sharply at night, especially considerably around 3 o'clock at night, which coincides with the time of the most diminished physiological reactions. In connection with what was outlined, of course, the need arises for the elaboration of measures which--by way of raising the physiological functions of the organism, especially the activities of the higher sectors of the central nervous system, would permit to make nightwork less harmful for health and at the same time more productive.

While solving this problem in a wide plan, finally we should at once reject as non-physiological the suggestion about the possible use of various medicinal stimulants for this purpose, and we should turn to such elements as work conditions, physical culture and, ultimately, nutrition.

In our investigations, our attention was concentrated on the role of nutrition as a natural physiological factor, having a powerful effect upon different functions of the organism and being capable to change the functional state of a few physiological systems of the organism in a desired direction.

We were especially interested in the nutrition problem in the plan of working up questions on the physiological composition of supper. Sleep is a natural physiological status of man in nighttime. The importance of sleep is huge for the organism. A man spends approximately one third of his life in sleep. Experience in life shows that the character of food used during suppertime leaves a certain impression on the sleep movement. But meanwhile, the solution of a number of practical problems about the best possible composition of supper remains completely empirical at the present time.

Medical practice is full of examples when the course of a number of ailments exacerbates at nighttime:-- vascular disorders develop frequently (hypertensive crises and infarctions of the myocardium); in peptic ulcer patients the pain becomes stronger; in bronchial asthma patients, asthma attacks become more frequent, and so on.

And meanwhile, our concepts about the pathophysiological mechanisms which are the basis of the mentioned disturbances are entirely imperfect, which ultimately will adversely affect the elaboration of pathogenetic therapeutical methods.

Study of all these problems is unthinkable without consideration of the circadian periodicity of physiological functions in the human organism.

In this monograph, the authors deal with the results of their almost fifteen-year' clinical investigations.

Human observations are the final stage in the chain of a biological experiment. "Nothing has the right to become a clinical rule on the basis of physiological alone; everything should be verified by clinical observation...".<sup>1</sup> With the modern methods of functional examination, the difficulties are, of course, very large in this respect.

The authors believe that the book will be useful for internist, dietologists, professional pathologists, and some other specialists who work on the problem of sleep, nutrition, and work organization.

The authors are thankful for all remarks of the readers, and they hope that these critical remarks and benevolent advices will help further on to eliminate the shortcomings in the work and to find more correct roads in solving the discussed problem.

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<sup>1.</sup> I. P. PAVLOV: Poln. sobr. tr., 1946, vol. II, p. 307.

#### CONCLUSIONS

(Results and Prospects of Future Investigations)

Extensive data in the literature and the material of our numerous observations show that in the course of a 24-hour day, almost all physiological functions of the organism experience a definite rythmic variation. In the human organism and in animals, perversions of the circadian rhythm of physiological processes are attained with some difficulty, although partial disturbances of the rhythm are also not a rarity.

Indeed, for the perversion of the circadian periodicity of physiological functions, investigators turn to such methods as the almost complete isolation of the organism from outside stimuli, marked change in the conditions of existence, for instance, keeping the animals in darkness from the time of their birth, or, on the contrary, under constant illumination (O. P. SHCHERBAKOVE, 1949; G. M. CHERKOVICH, 1950, 1953,; WOLF, 1930, and others). Perversion of the circadian rhythm in man is sometimes observed at time of transition to a steady nightwork (E. I. BRANDT & O. I. MARGCLINA, 1949, 1954; POLIMANTI, 1914, and others). If such disturbances of life routine are episodic, then, even under industrial conditions, during work performance, the course of physiological functions in the organism at nighttime remains as before, i. e., characteristic for the sleep state.

The cyclic changes in the organism are most distinctly shown in the activity of the central nervous system. The extreme functional manifestations of this periodicity are wakefulness and sleep.

Sleep is a peculiar adaptative mechanism which protects the central nervous system cells from exhaustion.

During sleep, the regulating role of the higher sectors of the central nervous system is not turned off, but it acquires a different, original character where an important role belongs to the inhibitory process. "Of course"--pointed out I. P. PAVLOV---"if the animal is sleeping, the complicated life of the apparatus mass continues, and not only does it continue, but it is not even disturbed, in spite of some signs of dormancy. In that case, well then, the nervous system both stimulates and inhibits during sleep. sleep...."

Sleep inhibition is the end result of the decrease in cerebral cortical excitability which is seen in the evening

-6-

hours and which we especially noticed when examining healthy people by the method of adequate optical chronazia. It should be emphasized that the degree of decrease in cerebral excitability in the evening hours is an integrated manifestation of the effect of various factors (favorable and unfavorable) of the surroundings upon the organism, and thus it is the result of the central nervous system's daytime work. Therefore, a study of the degree of decrease in cerebral excitability in the evening hours, with consideration of the nature of completed work, rest and nutrition during daytime, opens a promising wide field in hygienic investigations for the best and most useful shaping of peoples' lives.

In this respect, the findings are of special interest which we gathered on the functional state of the circulatory system at nightwork; for, it is unquestionable that blood circulation---which is to provide an optimum level of metabolism in every organ and tissue--generally reflects too well the characteristics of the functional state of the organism. Combined hemodynamic examinations made with the mechanocardiographic method of N. N. SAVITSHIY showed that, in reactions of the circulatory system to loading, there are substantial differences in daytime and at night.

While daytime work performance is accompanied by a slight rise in the systolic (lateral and terminal) pressure in absence of substantial changes in the distolic and mean homodynamic pressure, at nighttime, the same work occurs with a drop in all indices of the blood pressure.

In daytime work, acceleration of the pulse rate is usually seen, while at nightwork, it slowing is noted.

Thus, nightwork is carried out at such pressure levels and pulse rates which correspond to the ordinary circadian rhythm of these indices, i.e., to a "non-working," sleepy state of the organism.

In agreement with the usual circadian rhythm, at nightwork, the tonus of arteries and arterioles is lowered; therefore, the velocity of pulse-wave propagation and the specific peripheral resistance is diminished. However, in case of bradycardia, reduction of the blood pressure, lowering of the vascular tonus and an increased passability through the rise in the systolic and minute volume of the blood, manifested much more distinctly and to a greater degree than at the performance of the same work in daytime.

-7-

Thus, nightwork occurs with an entirely special state of hemodynamics:--increased minute volume of blood, i.e., an overall increase in cardiac work, with a drop in vascular tonus and reduced blood pressure.

Ordinarily, such a relationship of the mentioned hemodynamic indices is characteristic for states of hypotonis (N. S. MOLCHANOV, 1962).

The available findings permit to conclude that nightwork itself is accompanied by a certain perversion in the circulatory regulation, evidently caused by the influence of the dynamic routine of circadian periodicity of the physiological functions, combined with an increased demand for blood supply to working muscles, to the central nervous system, and other organs and systems. In case of systematic and prolonged nightwork, there will be either a perversion of the usual circadian rythm of blood circualtion (E. I. BRANDT and O. I. MARCOVINA, 1949, 1954; YE. L. SKLYARCHIK, 1960; POLIMANTI, 1914, and others), or a "breakdown" of the apparatus which regulates the blood circulation, and for this reason a state of sickness will develop. This is convincingly shown by the above quoted findings of A. P. GOLIKOV (1959) on the high incidence of high-blood pressure cases among peoples who systematically perform service obligations in nighttime. This circumstance urges to pay more attention to the problems of preventing cardio-vascular dystonias among night-workers. It is desirable that contingents of persons who, due to necessity, are obliged to engage in nightwork be taken under special medical control so that disturbances in the neurohumoral regualtion of blood circulation could be detected as early as possible and corresponding preventive steps could be made.

The functional state of the system of external respiration is also subjected to circadian variations. It was indicated above that, according to the data in the literature, during night sleep, the respiratory rate drops, the minute volume of breathing diminishes, the carbon dioxide content in the alveolar air increases. These findings were also corroborated in the investigations made by YU. I. KARETIN (1959) under our guidance. The indicated changes in the function of external respiratory system are also evidently caused by the sleep inhibition of the cerebral cortex, since a certain relationship can be noticed between the state of excitability of the respiratory center and the depth of sleep---in deep sleep, the excitability of the respiratory center is considerably reduced, which goes with an increase in the carbon dioxide tension in the alveolar air. A certain regularity is noticeable under the effect of sleep in the character of changes in the function of the orand of the digestive apparatus. The most distinctive changes are found in the function of salivary glands which are characterized by a marked drop in the reaction to neuro-humoral stimuli (pilocarpine), and by the absence of reaction to natural stimuli. The very marked inhibition of the activity of salivary glands is completely logical biologically:--during sleep they do not take part in the digestive function. But in time of awakening, the secretory reaction of salivary glands to the action of natural stimuli happens to be even somewhat higher than in daytime hours.

For more than half a century, a discussion has been running on the pages of the Press about the mechanism of the night secretion of the human stomach. Above, we showed that at the study of this secretion many investigators permitted substantial methodological errors which are necessarily reflected in the research results, and led to different concepts in regard to the causes and nature of secretion peculiar to healthy and sick peoples.

First of all, two concepts should be strictly discriminated:--the secretory reaction of the stomach at night to the effect of natural stimuli, and the secretion of an empty stomach, the secretion outside the digestive period.

Our investigations showed that in healthy persons, the gastric juice secretion gradually subsides from hour to hour; while, despite the presence of gastric sound, it stops almost completely during sleep. Upon awakening, the secretion of the the juice appears again, and it increases in the morning hours. Reduction of the secretion in the late evening hours, the almost complete stoppage of secretion during sleep, and the increase in juice secretion, let us say, without visible causes in the morning hours--all proves, that outside the digestive period, the secretory activity of gastric glands, and that of the salivary glands, is closely related to the function of the higher sectors of the central nervous system. It is a reflex, by its nature in particular, a conditioned reflex activity. With these theses, we can easily explain the more abundant secretion of gastric glands in the evening hours, their subsequent slowing down at the moment of saturation (decline in the excitability of the cerebral cortex), and its marked increase in the morning hours, when conditioned-reflex influences of the external environment increase and conditioned reflexes get the overhand. The possibility that conditioned reflexes can be formed to time was demonstrated by a number of coworkers of I. P. PAVLOV and K. M. BYKOV (Yr. P. PEOKRITCVA, 1912; M. M. STUKOVA, 1914; V. S. DERYABIN, 1916 and A. D. SLONIN, 1935, and others).

Thus, there are no reasons to maintain that a continous secretion of the gastric glands, under any conditions, is peculiar to man:---the secretion of gastric juice is only in response to stimuli. This conclusion is in good agreement with numerous experimental findings of 1. P. PAVLOV's school.

The discussion of the results of this series of investigations on this topic could be stopped, since the changes in secretion are so much stereotypical, and are repeated so much in every detail from one examination to the other, that they do not call for any doubt. But there is one methodological detail which merits discussion. The last intake of food in our examinees was at 14:00 o'clock, which is unusual for the food regime of a healthy man. This is also why the question comes up, how do the gastric glands secrete at night if the last food intake occurs, not at lunch time but at supper time as is the usual in life. Specially made examinations assure that, in healthy people, the character of nocturnal gastric secretion depends to a considerable extent upon qualitative characters of the food consumed at supper. If the food is rich in extractive substances (bouillon), or it contains much salt, then in healthy persons, gastric juice is continuously secreted at night. But after the consumption of dairy products at supper time, nothing similar is observed. In this case, at the hours of the usual reduction of secretion (from 2 to 4 o'clock at night), the stomach is almost always empty.

Without being concerned now with the mechanism of action of the indicated food articles upon the secretory function of the stomach, we mention only the fact, that in healthy persons, the formation of gastric juice is not inhibited by sleep. In response to the action of stimuli, the gastric glands react with secretory response. Is the distinct secretory reaction of gastric glands maintained for all stimuli during sleep? The solution of this problem is not only of a theoretical importance, but makes possible certain recommendations, in the composition of a very useful nutrition.

Having taken advantage of the method of K. M. BYKOV and I. T. KURTSIN, with the use of a series of chemical stimulants, we were able to find, that in healthy persons, during sleep, outside the digestive period, the gastric glands are in a state of relative rest, while--in difference from the salivary glands--remaining always sensitive to various secretory stimuli:--both neural (mechanical stimuli) and humoral (alcohol, cabbage juice, meat bouillon) stimuli cause an abundant gastric juice secretion. These findings point out that sleep inhibition, which develops in the higher sectors of the central nervous system, does not spread to the secretory centers of gastric glands. But it does not follow from this that the neural secretory centers of gastric glands do not experience any effects on the part of developing sleep inhibition.

Study of the functional activity of gastric glands, both during the day and or night, showed that in healthy persons, the first complex reflectory phase of gastric secretion is somewhat inhibited compared to the daytime, while the second neuro-humoral phase displays a distinct trend toward rising. It seems to us that a single, very important rule follows from these observations for the composition of the most useful nutrition. The food which is consumed at suppor time should contain sufficient amount of substances which stimulate the neuro-humoral activity of gastric glands. In this case, first, the food will be well digested, which assures sufficiently large secretion of gastric juice, and, second, impulses of reflectory stimulation of julce secretion from the gastile receptors will enter into the higher sectors of the central nervous system with limitation, to wit, such impulses which coold from additional foci of stimulation in the subcortical centers and thereby, hinder the propagation of sleep inhibition. Consequently, when planning the evening meal, not only the volume of the meal should be considered (there is no doubt that the stonach interferes with the development of a lasting and healthy sleep, especially in elderly persons), but the qualitative composition of the food should be taken into consideration. If the question on the physiological foundation of the qualitative properties of supper is to be solved only from the standpoint of the secretory activity of the stomach, then preference should be given to food at suppor time which would be processed in the stomach chiefly at the expense of the neuro-hudoral phase of secretion. By the way! Let us mention that an increase of the second, neuro-humoral phase of secretion can be observed not only during natural, but also in medicinal sleep (ME. B. VYGODNER, 1952; N. I. LEPORSKIY and YE. A. NECHAYEVA, 1957), which is important to be considered in the organization of nutrition during sleep therapy. However, not all food articles, rich in neuro-humoral stimuli for gastric secretion should be recommended for sonsumption at supper time.

There will be no doubt that if at suppor time a food is taken which is rich in extractive substances and salt then unfavorable conditions are being created for the activity of the stonach:---the empty stonach accretes during the whole night. If, however, dairy products are taken at supper, then the functioning status of the stomach, including also the subsequent secretion, is shorter in time, and the gastric glands enter into a state of relative rest earlier than after

-11-

bouillon con umption. The literature has indications that, in the case of digestion of milk and dairy products, the largest amount of gastric juice is excreted in the first two hours of the dood's stay in the stomach (I. P. PAVLOV, I. YU ROMANOVA et al.).

Thus, by studying the character of the secretory activity of the stomach, at supper time it is more advantageous to take dairy products, and no food articles rich in extractives and salt. It is quite natural that very complicated questions cannot be solved only with the consideration of the activity of gastric glands. On this problem we shall still say something below.

Organs of the hepato-pancreatico-duodenal system have little change at night, including also the period of sleep, in the functional activity which is peculiar for them in daytime. In man, the periodic secretory-motor activity at night, is of the same character in principle as in the daytime. During sleep, when the conditioned-reflex ties of the organism are disrupted by the surrounding environment(including the pathological medium, and then the condition is reduced, the function of the organs of the hepato-pancreatico-duodenal system becomes, perhaps, less marked, but more distinctive and regular.

The above outlined facts serve as a basis for the supposition that, in healthy people in sleep, food digestion in the gastro-intestinal tract is going on rather intensively.

During a 24-hour day, considerable changes are also seen in metabolism:--thus, the majority of investigators points out the decline in the blood sugar level during night sleep. Data are available on the reduction of inorganic phosphorus level at the same time(H-1DANE, 1924). At night, the maganese, silicium, copper, aluminium content of the human blood increases (YE. V. SABADASH, 1959).

Investigations of V. I. OVCHAROV, who worked under our guidance, permitted to detect a tendency to an increasing prothrombine level in the blood in the evening hours.

Nobody doubts the theoretical and practical importance of a study of the circadian rythm of physiological (vegetative) functions under pathological conditions in various ailments.

It is well known for the clinicians that deterioration of the condition of patients, or complications in a number of ailments, develop at a certain time of the 24-hour day. In the evening and night hours anginal attacks, paroxisms of bronchial or cardiac asthua, and so on, are more frequent than during daytime.

And what is more, the development of exacerbation of a pathological process at night helps to a certain extent in differential diagnostics, as, for instance, thrombosis of cerebral vessels usually develops at night in difference from cerebral hemorrages, while the painful syndrome at this time of the 24-hour day in peptic ulcer is characteristic for a localization of the ulcerating process in the duodenum. Experience in emergency and first aid medical work proves that the number of calls increases considerably in the evening and at nicht. To become convinced that there is some sort of regularity in the development of pathological conditions which require emergency medical aid, depending upon the time of the day, the works of emergency service posts of two policlinics of the Moscow Rayon in Leningrad were thoroughly analyzed. The data which characterize the number of calls according to emergency service in the time from 1 September to 15 December 1983, are given by the material of one of the Leningrad policlinics in Table 38.

TABLE 38

WORK PERFORMANCE OF EMURGENCY STATION				
		9-18 o'cl.	18-24 o'cl.	0-9 o'cl.
Number of c	alls	412	632	340

As it can be seen from Table 38, during the indicated period, the total number of calls was 1384. Of these, 632 patients (45.5%) were attended at home during the time from 18 to 24 o'clock; 412 patients (29.7%) were treated in the daytime, and 340 patients (24.5%) were treated in the hours of night. Thus, the largest number of calls for emergency service occurs in the evening hours (18 to 24 o'clock), despite the fact that this time interval includes only 6 hours.

Table 39 gives the findings on the work of the emergency station of another policlinic.

TABLE 39

(Number of calls)				
YEARS	Total calls in		Time	
	24 hours	9-18 h.	18-24 h.	0-9 hr.
1959 1930 1961 1962	5,798 5,803 6,095 5,749	2,224 2,132 2,307 2,117	2,208 2,218 2,371 2,204	1,363 1,403 1,417 1,407
10tal	43,490	ະ, ແມ	0,001	5,594

WORK PERFORMANCE OF EMERGENCY STATION (Number of calls)

As it can be seen from the Table, the number of calls is approximately the same in the daytime and in the evening. However, if we consider that the daytime period (9 to 18 o'clock) is longer than the evening period (18 to 24 oclock), then the largest number of calls was received in the evening. This becomes especially noticeable if we consider the circumstances that the evening time (18 to 24 o'clock) is much less than the daylight and the night periods of the 24-hour day. Thus, as an average, the number of calls per hour of daylight time was 988.8, in the evening it was 1500.1, and in the period after midnight it was 621.5 per hour.

The opinion exists that patients die more often at night, or in the early morning hours. For instance, TREU (1930) found that in postoperative patients, death more frequently occurs at night than in the daytime. In this regard, findings of the University of Magdeburg (1935) are of a certain interest whose collaborators analyzed 3507 fatal cases, and arrived at the conclusion that the largest number of death occurs in the early morning hours; patients died most infrequently at noon. P. P. LASAREV (1947) came to the conclusion on the basis of adequatometric data that the sensitivity of the brain is lowest between 3 and 4 o'clock at night, and highest at 14:00 o'clock in the afternoon. In correspondence with this, the author stated that the fatality increase in the night hours is conditioned by the marked lowering of the brain's sensitivity. However, WIGAND (1935), who studied mortality in internal diseases (672 fatal cases), found that in the period from 18:00 o'clock until 6:00 o'clock in the morning, the mortality rate was only 10% higher than in the daytime.

We analyzed the case histories of 2323 deceased patients in one of the large clinical hospitals of Leningrad for the 1952 to 1960 period. This group did not include cases of death from poisoning, or cases in which death occured on the first day of the patient's stay in the hospital. The obtained data are given in Table 40.

As it can be seen from the Table (on following page), the number of fatalities was the same in daylight (10-17 o'clock) and nocturnal (0-7 o'clock) hours. Patients rarely died in the period from 17 to 24 o'clock. Consequently, we did not see any regularity in the occurrence of fatal outcome among the patients with internal diseases which would be related to the time of the day.

It should be mentioned that in the group of patients who died between midnight and 7 o'clock, the largest number of death occurs in different ailments. Thus, in diseases of the cardiovascular system, patients die more often at night, in malignant tumors and blood diseases, they die in the evening. In other disease categories, death occured more frequently in the daytime.

NUMBER OF PATTEURS WHO DIED AT DIFFERENT

TABEL 40

	HOURS OF THE DAY				
Dis	sease category	7-10	10-17	17-24	7-0
	an ge gan bri be min d'r go bri o'r ddynam aprilleg ar rhy goryn y	0'cl.	o'cl.	o'cl.	o'cl.
1.	Diseases of the cardiovascular system	70	237	223	262
2.	Diseases of the external respira- tory system	32	122	94	116
3.	Diseases of the di- gestive system	10	40	25	33
4.	Renal diseases	5	19	19	15
5.	Diseases of the blood	8	13	18	12
6.	Mallynant tumors.	96	233	256	232
7.	Other diseases	22	39	34	37
TO	PAL	243	703	669	708

Our observations permitted to say that, in hypertensive patients, the excitability of the higher visual nervous centers is much more reduced than in healthy person, moreover, in the late stages of the ailment, the lowering of excitability increases. In hypertensive patients, the largest indices of adequate optical chronaxia (=AOCn) were observed in the morning hours, in difference from healthy persons in whom the largest indices of AOCn were noted between 2 and 3 o'clock at night.

Perversion of the circadian rhythm of the indices of adequate optical chronaxia was also observed in peptic ulcer patients (gastric and duodenal ulcer. In difference from healthy persons, the night drop in the excitability of their

-15-

higher sectors of the central nervous system is much less marked. We studied the hemodynamics at night in hypertensive and peptic ulcer patients with the mechanocardiographic method. We could notice a substantial perversion of the circadian rhythm of hemodynamics in this category of patients. Thus, in hypertensive patients in the initial stages (I and II A by the classification of A. L. MYASNIKOV) the diminution of peripheral resistance, bradycardia and drop in the blood pressure at night is associated with a substantial increase in the systolic and numute volume of blood, and with some increase in the tonus of the muscular arteries. This increase in cardiac work, inadequate to the needs of the organism, is evidently caused in these patients by the absence of the drop in the excitability of the central nervous system which is seen at night in healthy persons. In this connection, the hemodynamic investigation is in agreement with the above quoted data obtained with the method of optical adequate chronaxia.

In patients with high blood pressure, in stages II B and III, the perversion of the circadian rhythm of hemodynamics is still more markedly expressed. At night, such patients experience not a drop (as in the healthy persons) but a rise of all indices of the blood pressure, increase in peripheral resistance, reduction of the systolic and minute volume of the blood. The mentioned hemodynamic shifts evidently play a substantial role in deterioration of the condition of hypertensive patients at night, in the increased frequency of anginal attacks in such patients, in cerebral disturbances, and fatal outcomes. This is proved also by our findings on the diminution of oxygen saturation of the arterial blood in hypertensive patients, especially at night.

Examination of the night hemodynamics in peptic ulcer patients (gastric and duodenal) permitted to find perversion of the circadian rhythm of their hemodynamics, resembling much the hemodynamics of healthy people, but in a number of cases, the blood pressure even increased, the blood circulation deteriorated in the precapillary system, the systolic and minute volume of the blood increased.

The similar character of hemodynamic changes in hypertensive and peptic ulcer patients is in agreement with the findings obtained with the ACCh method, and which prove the excited condition of the central nervous system, and, in particular, of the vasomotor center at night in these ailments. The similarity of hemodynamic changes in case of hypertensive and peptic ulcer patients is still another proof for definite relationship of the cortico-visceral genesis of both ailments in which disturbances of the neuro-humoral regulation of blood circulation are playing an important role.

Both the data in the literature (A. A. STUPNITSKIY, 1956), and the investigations which were made under our guidance (V. A. SHAYDENKO, I. A. GLADYSHEV, YU. I. KARETIN and V. A. PRIKHNO) point to a disturbance in the functional status of the external respiratory system during sleep in cases of different ailments, and particularly in hypertension with attacks of angina pectoris and infarction of the myocardium. Changes in the rate, rhythm, and depth of respiration are combined in such patients with lowering of the oxygen content in the arterial blood. In individual patients with acute infarction of the myocardium, during night sleep a Cheyne-Stokes type of transitory respiration was recorded. In hypertenseve patients, in difference from healthy peoples, the depth of respiration was reduces at night, the reduction of its rate and the diminution of the minute volume of respiration was less marked.

Investigations of V. I. OVCHAROV and V. S. PRIKHNO, which were made at our suggestion, permitted to notice a rather frequent drop in the prothrombine level of the blood at night in hypertensive patients with chronic coronary insufficiency.

Chronic gastritis patients, and especially peptic ulcer patients with localization of the morphological changes in the duodenum, showed at night, outside the digestive period, a copious continous gastric secretion. Under the effect of sleep, the juice secretion is sometimes a little decreased in volume, but it does not fully stop, while in patients with duodenal ulcers, an increase in the volume of secretion can be even observed during nocturnal pains.

Consequently, the two main factors---namely, presence of chemical irritants and conditioned-reflex influence of the surrounding environment which, even in healthy peoples, are capabel of provoking a prolonged gastric juice secretion at night---cannot be referred to for an explanation of the continuous secretion of gastric glands which is peculiar to some patients who have chronic gastritis, gastric ulcer, and especially duodenal ulcer.

These facts harmonize will with the concept about the presence of persistent foci of stimulation in the subcortical secretory centers of these patients. The developing sleep inhibition is not in a state to fully suppress the functional activity of the mentioned foci, which is also manifested by the special state of hemodynamics and gaseous metabolsm and the continuous gastric secretion. However, in some cases, the developing sleep inhibition induces these foci of excitation even favorably, which in manifested by a still greater intensification of the mentioned changes in the vegetative functions. The data of modern morphology and neurophysiology make tangible our concepts on the localization of the foci of pathological excitation in peptic ulcer patients.

When they studied the role of the hypothalamopituitaryadrenal mechanism in the regulation of the secretory activity of the stomach, FRENCH and MAGOUN (1952) and others established that the anterior hypothalamic region acts through the vagus nerve, while the posterior region acts through the pituitary and the suprorenal cortex, and it causes the so-called delayed secretion of hydrochloric acid. By a prolonged irritation of the hypothalamic region with implanted electrodes, in experimental animals, FRENCH, PORTER and others (1954) provoked not only a continuous secretion of the gastric glands, but also the development of ulcers in the stomach and duodenum.

These facts served as a basis for some investigators, especially American researchers, to advance a new, endocrine theory of the pathogenesis of peptic ulcer (FRENCH, LONGMIRE et al., 1953; FRENCH, PORTER, et al., 1954; SHAY et al., 1958).

The findings of the quoted authors permit a high estimation of the role of hormonal factors in peptic ulcer genesis. However, starting from the concepts of our native scholars about the function of the organism, these findings should be considered in the light of a primary disturbance in the function of higher neural regulatory mechamisms.

Table 41 includes data on the degree of diminution in volume of nocturnal gastric secretion in healthy persons during sleep compared with the period of wakefulness. From the data of the Table it can be distinctly seen that under the influence of sleep inhibition, in patients with peptic ulcer, especially in patients with duodenal ulcer, the volume of gastric secretion decreases to a smaller extent than in healthy persons.

In agreement with the Favlovian concept on sleep, all these facts prove that in peptic ulcer patients, the inhibitory influences of the cerebral cortex become weaker on the subcortical secretory centers. Consequently, a study of the functional state of the stomach in sleep can be used as an objective method for the evaluation of cortico-subcortical interrelations.

By playing a substantial role in the vital activities of the organism, none the less, circadian changes of the physiological processes are still insufficiently taken into account in the solution of many practical questions.

-18-

## DEGREE OF DIMINUTION OF THE VOLUME OF NOCTURNAL GASTRIC SECRETION DURING SLEEP COMPARED WITH THE PERIOD OF WAKEFULNESS (in %)

TABLE 41

GROUP	<ul> <li>Degree of dinimution of secretion</li> </ul>
Healthy persons	74
Chronic gastritis patients	58
Peptic ulcer patients:	
Gastric ulcer	60
Duodenal ulcer	45

Today it has already become obvious that a correct organization of the regime of work, rest, and nutrition cannot be imagined without consideration of the characteristics of the routine in organismic function, in particular without the consideration of the circadian variations of vegetative functions and especially of the functional state of higher sectors of the central nervous system; for, the rhytnmic course of physiological functions in the organism is determined to a great extent by the alternation, sometimes of stimulatory, sometimes of inhibitory processes which prevail in them (K. M. BYKOV and A. D. SLONIM, 1960). Both the regime of work, rest and nutrition, and the therapeutical action upon the organism of the sick man should be constructed with a consideration of the circadian rhythm of physiological functions.

It should not be thought that these peculiar features in the secretory activity of the stomach which are found in peptic ulcer patients at night, are something entirely exclusive, characteristic only for this ailment. Often, they are manifested in chronic gastritis patients, and sometimes, even in healthy persons. In the latter case, they can be caused by peculiarities in the food ration. For instance, with the supper-time concumption of a large amount of salt, or of products rich in extractives, in healthy persons during the whole night, abundant gastric secretion is observed, moreover during sleep, the juice excretion and acidity

-19-

can even be considerably increased, resembling the gastric secretion in peptic ulcer patients. At a still more distinct degree, the nocturnal gastric secretion increases in chronic gastritis patients if they consume salty food at supper time. Consequently, a badly chosen nutrition can elicit or maintain an already developed cortico-subcortical disturbance, it can contribute to the exacerbation of desease and to its further evolution. However, there is still much to do for studying the effect of the supper's qualitative properties upon the course of the pathological process in peptic ulcer and in hypertensive patients. It seems to us that the work in this research area is very promising.

Our material makes possible to determine the basic principles of a physiological, reasonable composition of supper for healthy persons.

During a work day, the organism spends a large amount of energy. The power resources, in particular, the glycogen reserves, become exhausted. Consequently, for the replenishing of these reserves, the organism needs carbohydrate influx. Furthermore, there is a ground for the supposition that at night, regenerative processes occure also elsewhere than the carbohydrate metabolic sphere. As our investigations on the determination of some nitrogenous components (total nitrogen, amino acid, nitrogen, urea) proved, plastic processes and such types of metabolism go on actively at night in which protein components take part. A. S. KONIKOVA and her coworkers at Prof. A. A. Visnevskiy's clinic established with the method of labelled atoms that during medicated sleep, the protein metabolism is increased because the protein synthesis is more intensive in the tissues and organs of the animal organism.

One ought to suppose that only a thorough study of the characteristics of metabolism occurring in sleep can answer the question what the composition of supper should be in regard to chemical ingredients. Undoubtedly, this is a very important and extensive biochemical problem. In our investigation, we dealt with it only in a general way. Nevertheless, even today, starting from the above outline, the first rule for the qualitative composition of supper can be formulated in the following manner:--food articles which are included in the composition of supper should assure the normal course of restorative and plastic processes activated in the human organism at night, especially in sleep.

A certain degree of fatigue of the higher neural centers and the subsequent drop in their excitability is a necessary condition for the development of sleep. In the evening, the excitability of the higher sectors of the central nervous system is lowered, and thereby, conditions are created for the development of inhibitory reactions and of sleep. As indicated above, the act of eating and the subsequent digestion have a substantial effect upon the functional state of the central nervous system. After the intake of some substances (sugar, chocolate, coffee, strong tea, and so on), cerebral excitability is considerably increased, while after the intake of other substances (milk and dairy products, meat and fatty food), cerebral excitability is lowered for a certain period of time, and thereby, conditions are created for the development of inhibitory irradiations. Hence, here is the second rule for the physiological composition of supper:-supper should consist of such food articles whose intake is followed by a drop in cerebral excitability, and not by an increase.

What requirements should supper satisfy, starting from a consideration of the characteristics of the nigh tion of the digestive apparatus?

In the night hours, the salivary glands respond with a distinct secretory reaction to natural stimuli. However, in sleep, the salivary gland function is inhibited, and these glands do not participate at this time in the digestive process. Therefore, the above raised question should be answered with regard to the functional characteristics of the lower sectors of the digestive apparatus, and first of all of the stomach.

In a large series of examinations, we showed that at night, the first complex-reflex phase of gastric secretion is inhibited. This is the phase which is provided by the participation of predominantly neural mechanisms. On the contrary, a tendency is found to increase the second, predominantly humoral phase of secretion. From this, the following third rule is derived for the physiological composition of supper:--at supper time food articles should be taken for whose digestion the secretion of gastric juice is conditioned by means of a predominant excitation of the humoral chemical mechanims (and not of the neural mechanisms) of gastric gland function.

In this case, firstly, the food which enters the stomach will be well worked up with juice, and, secondly, a stream of interoceptic impulses of the nervous stimulation of gastric secretion will be here limited in the higher sectors of the central nervous system, which will help the development of sleep inhibition. But by this consideration, the old rule also remains in force that supper should not be overabundant in volume, it should not overfill the gastrointestinal tract, the processing of the food articles should not be accompanied by superfluous gas formation, and so on, for all this will reinforce the stream of interoceptive signaling, and will disturb the development of sleep.

Under the effect of sleep the motor and evacuatory functions of the stomach are not changed substantially. At night, the hepato-pancreatico-duodenal system maintains a high-degree of functional acitvity. All this points to the fact that the food arriving from the stomach will be thoroughly, and rather intensively, worked up in the lower segments of the digestive apparatus.

The processing of food articles in the gestro-intestinal tract, and the more so the processes of tissue metabolism, take a long time, indeed different time for the consumption of different products. Thus, leukocytic reaction seems to depend upon the quality of consumed products after three and even five hours, while the signs of the specific dynamic effect of food, manifested by the degree of energy stress of the organism after digestion and assimilation of food substances, are clearly detectable 4-6 hours after food intake. It should be kept in mind that after taking the same food, didestive leukocytosis and specific dynamic effect of food occur more often later at night than in the daylight hours. This finding indicates that the process of final utilization of food substances is draged out at night. When, for instance, meat products are consumed at supper, an intensive metabolic process is found even at the late hours of night when many physiological systems usually lower their functional activity. Parallel with high energy losses, unusually for this period of tiem, the pulse rate, respiratory rate and the blood pressure level are changed. Of course, all this is going to hinder the normal course of restorative processed and sleep. Hence, we have the following rule for the physiological construction of supper: -- supper should consist of such food articles whose processing in the digestive apparatus and the process of terminal assimilation of their decomposition products would go on with the smallest energy loss by the organism and would be completed in a comparatively short period of time.

Now then, what kind of articles should be consumed at supper time? In the final analysis, this question ought to be solved with the consideration of many factors, for instance, age, characteristics of work activity, climatic conditions, and so on. Our material permits more or less definitely to speak only about the question of the protein components of meals. In this regard, only a single opinion is possible:-preference should be given to dairy products, and not to meat products. The supposition on the physiological characteristics and appropriateness of consuming dairy products at supper time is entirely in agreement with the peculiarities of organ and system functions of the organism at night.

Indeed, after taking milk and dairy products in the evening hours, the excitability of the higher sectors of the central nervous system appears to be lowered. In fact, lowering of the excitability of the cerebral cortex is also observed after taking meats and fatty meels. But it would be hardly correct to solve the question about the suitability of consuming such or similar other products at supper only with consideration of the primary reaction of the central nervous system. Nevertheless, we emphasize that after the consumption of milk and dairy products, the excitability of the cerebral cortex is lowered, and as a result, conditions are created for the development of sleep inhibition. By the way! Let us mention that A. A. OSTROUMOV (1903), eminent Russian clinician, pointed out in his "Clinical Lectures": "Milk has a good effect, by suppressing an irritated state of the nervous system."

The physiological foundation of dairy products consumption at supper time is especailly clearly revealed at the investigation of the question from the viewpoint of the function of the gastro-intestinal tract. As it has been stated above, food articles used in supper should be processed firstly, by digestive juices conditioned chiefly by excitation of the humoral mechanisms of gastric gland function, secondly, with the smallest stress of the glandular apparatus, and thirdly, the process of working up food substances should be completed in a comparatively short time.

I. P. PAVLOV indicated that "milk is in an exceptional position among the kinds of human meal." I. P. PAVLOV motivates this exceptional position of milk by three features. Firstly, the weakest gastric juice is poured out on milk, and also the smallest amount of pancreatic juice in comparison with other food articles, for instance, with meat and bread, taken in amounts equivalent as to nitrogen. Furthermore: "Milk has another important property:--introduced directly into the stomach, imperceptibly to the animal, it always causes a certain degree of secretory activity of the stomach and pancreas, i.e., it is itself a chemical stimulus for the digestive canal." I. P. PAVLOV repeatedly emphasized that "in truth the secret of milk is that no substantial difference is noticed in the discharging work of the digestive canal, whether the milk is put into the stomach without the animal's knowledge, or it is fed directly to the animal. For meat, although it is the best chemical stimulus, the mode of its

entry into the stomach....is of great importance."1

According to the findings of G. N. OKROVSKIY (1924), N. P. RASUMOV and F. M. LEVIT (1927), A. V. SOLOV'YEV (1959), the juice-producing effect of milk is caused by the presence of some substance in the milk serum which is resistant to culinary treatment, and which stimulates the neural mechanism of gastric function. This is why a high-grade juice-producing effect is characteristic, both for whole milk, and also for dairy products such as kefir, sour milk and cottage cheese (I. M. GORDYEV, 1906; I. V. KAS'YANENKO, 1957, 1959). In view of the large fat content of sour cream cream and cheese, the period of juice secretion after these products is prolonged for a long time (I. M. GORDEYEV, 1906).

We should still say something about one particular characteristic of the function of gastric glands when milk and milk products are consumed. And this is the long duration of secretion. When feeding milk and meat in amounts equivalent for nitrogen, the secretion of gastric glands is not only more economical after milk intake, but it is also less prolonged than after meat intake. When milk and milk products are ingested, the gastric juice secretion stops shortly after the transition of food substances from the stomach to the lower segments of digestive tract, while, in cases of meat eating, since the meat is rich in extractive substances, the period of juice secretion extends over 6-8 hours.

In this regard, our investigations are also demonstrative in which we studied the character of nightime gastric secretion in relation to the qualitative characteristics of supper. As it was shown above, after the intake of meat bouillon at 21 o'clock, despite the absence of food in the stomach, the gastric glands continued their juice secretion even at 3-4 o'clock at night, when, parallel with lowering the functional activity of may physiological systems, usually also the secretory function of the empty stomach ceases. Another was our observation after the intake of kefir at supper time which has the most marked juice-producing effect among dairy products. In this case, the process of gastric digestion was usually completed at 3-4 o'clock, and the gastric glands reached a state of relative rest.

Milk products, in difference from meat products, are not only relatively rapidly digested in the gastro-intestinal tract, but, as our investigations showed on the study of leukocytic reaction and specific dynamic effect, they are also comparatively promptly assimilated by organs and tissues.

<sup>1.</sup> I. P. PAVLOV. Poln.sborn.tr., 1946, vol. II, p. 144.

Meat food is worked up by the organism with greater stress than the dairy product, and the biochemical processes for its ultimate assimilation stretch out over a longer period of time, as this is shown by gas analytical data. As our inves-tigations showed, if meet meal is taken at 21 o'clock, i.e., at the usually accepted hours of supper, then almost for the whole night, an increased energy spending of the organism is observed, while in the period from 2 o'clock to 4 o'clock, when many physiological systems reduce their activity, are still more distinct increase if often observed in the energy losses. Instead of a lowering, which is usual in these hours, the pulse rate, and respiratory rate, and blood pressure level ramain at high figures, and there is even a trend to their increase. But after the intake of equivalent amounts of dairy products, no similar observations can be made. In the hours of the usual lowering of physiological functions, parallel with the decrease in energy loss (approximately to the level of basal metabolism), the pulse and respiratory rates became less frequent, and the blood pressure dropped.

Metabolism, and consequently also the biochemical processes of the final utilization of food products, are reduced in their intensity during night sleep. This can be especially distinctly demonstrated on the example of sugar curves which, at night, acquire lines similar to diabetes. Therefore, it becomes clear why the gastric glands secrete gastric juice at night so long after the evening-hour intake of meat meal rich in extractive substances. It ought to be supposed that these substances circulate in the blood for a long time, and by a humoral way, they stimulate the gastric glands to activity. In milk and milk products, such substances are evidently not contained, and even if contained, they are present only in a small amount.

Thus, with dairy products, it is possible to introduce into the organism a sufficient amount of protein, and, evidently, the process of their working up in the organism will not hinder the development of sleep. Moreover, there is every reason to believe that sleep development and processing of dairy products in the organism are processes mutually strengthening each other. This close interaction between sleep and milk digestion is established in the organism of the child already from the first day after birth. You know, milk--the product prepared by nature itself, in early childhood, is first the only food product, and thereafter it remains one of the basic products in nutrition still for a long time. It is well known to all that after food intake (milk), a healthy child usually falls asleep. Under these conditions, between the sleep process and the process of milk assimilation, there are such physiological and biochemical interactions

-25-

(and they are inherited from generation to generation) which, in the best form, on the one hand, assure normal sleep and, on the other hand, guarantee a perfect run of the process of working over and ascimilating food substances by the organism. This close interaction between milk nutrition and sleep is so advantageous for the growing organism that the child doubles his weight in half a year.

In the ultimate analysis, we are far from the thought to believe that the requirements of an adult person for food articles can be completely satisfied with milk and milk products, although milk and milk products are exceptionally valuable food substances. As to completeness of composition, there is not a single natural food which could be compared with milk in this respect. Milk contains all the needed amino acids; it is rich in vitamins (B<sub>1</sub>, B<sub>2</sub>, PP and C) and mineral salts. Milk and milk products are widely used in therapeutical practice. In milk production, our country occupies the first place in the world. However, the facts point to an insufficient consumption of milk and milk products in the large cities of our country, chiefly by the adult population (R. B. DAVYDOV, 1958). This is explained first of all so that the population is not properly informed about the high nutritive value and other useful properties of milk.

Not to mention children, adult peoples should use milk and milk products daily. The above quoted materials give a basis for drawing a conclusion about the physiological motivation and suitability of consuming milk products, particularly at supper time. In the final analysis, supper should not be composed exclusively of dairy products. Starting from the need for restoring the energy reserves of the organism, especially of physical workers, dairy products at supper time should be combined with products rich in carbohydrates (groats porridge, potato, farinaceous products).

Let us now consider some problems related to the nutrition of persons who perform nightwork.

The problem of nighttime nutrition was not raised just today. In the U.S.S.R., it acquired importance in connection with the industrial development, with putting large factories and works into operation, which work almost with identical stress all around the day. By judging from the literature, the problem of nutrition is still only in its organizational plan. In their time, M. S. MARSHAK, V. L. OSTROVSKIY, and Ya. T. POLYACHEK (1940) considered that "for a long time public catering coped with this task, and worker at night shifts had hot dinner ("obed") in their meashall which did not differ at all from the food given to daytime shifts." Such a solu-

-26-

tion of this very complicated problem seems to be hardly correct, or scientifically grounded.

Our examination outline a few fundamental theses on the contruction of nutrition for nightworkers.

First of all, let us discuss the quantative side of nutrition. The findings which the present investigation obtained indicate that in doing the same work, the organism requires less energy at night than during the daytime. Even though this difference is small and equals only 8% as an average, it was statistically significant. Thus, the impression is created that in the work process, the organism spends energy at night more economically than in the daytime. This peculiar characteristic of nightwork should be taken in consideration at the solution of the quantitative problems of nutrition.

Despite the fact that the energy losses of the organism on physical load are lower at night than during the daytime, we are far from the thought to consider night hours better for work than daytime hours.

The lower expense of energy per work unit performed at night should be explained first of all with the lowered activity of many functions of the organism at this time: --the pulse and respiratory rate slow down, the muscular power decreases, the body temperature drops, the basal metabolism diminishes, and first of all the excitability of the higher sectors of the central nervous system is reduced. This diminution of the physiological functions of the organism at night is a sequela of the living routine. As to time, it usually coincides with the sleep period, but it is so sub-stantially complicated and regular that it is observed even when a person is not just awake at night but is even occupied in work. Since the higher sectors of the central nervous system remain inhibited at night to a certain degree, they are less reactive, less sensitive to stimuli of ever kind. Consequently, in this case, a reaction to a stimulus effect will be less generalized, not only within the range of the central nervous system, but also in the organism as a whole. In the required measure and coordination, not all organs and systems of the organism will compensatorily change their functional activity for a full assurance of one or another activity of the organism that developed in the work process. You know, it is perfectly clear that in an integral organism, at the presentation of increased requirements to any single organ, the other organs and systems of the organism do not remain indifferent. For instance, the work of lifting a load to a definite height is assured, not only with the participation of the neuro-muscular apparatus. This process can be

-27-

carried out for a long time only under the condition of a simultaneous corresponding compensatory functional reinforcement of the cardiovascular system (delivery of power material), of the external respiratory system (increased  $0_2$  supply and excretion of CO2), of the activity of the liver and other organs. The highest regulator of this orderly activity of the organism is the central nervous system. Therefore, the main condition of a perfect support of the working process is first of all, a rather high functional activity of the higher sectors of the central nervous system. It can be expected that in such cases when the higher sectors of the central nervous system are inhibited for one reason or another, when the excitability of the higher regulatory centers is raised, when these centers are hardly sensitive to signals about the need of compensatory reinforcement or relaxation of the activity of one organ or another or one system or another in the organism, --- each time the organism will not be able to productively participate in the work process to any length of time.

This night failure of the organism at prolonged loadings was especially distinctly manifested in our investigations in the determination of muscualr working capacity with the aid of a spring hand dynamograph. During this investigation, a limited group of muscles was subjected to loading, which made possible during a comparatively short period of time to track down not only the tiring process, but also the process of restoration of the working capacity. It was shown that muscular working capacity is considerably lowered at night, fatigue will quickly develop.

That the basis of lowered working capacity at night is the suppression of physiological functions conditioned first of all by the reduction of excitability of the central nervous system, and not a direct effect of the work itself, is shown by the observation when in nightworkers, the working capacity begins suddenly to rise in the morning without a preliminary rest period. The rise in muscular working capacity in the morning hours was repeatedly observed on himself by one of the authors of the present investigation (F. I. KONAROV).

Is it possible, with the aid of food substances with specially constructed diets, to make nightwork less harmful and at the same time, more productive?

Food is a powerful factor of action upon the organism, upon its metabolism and functional phenomena. Under effect of food, even the functional status of the higher sectors of the central nervous system will change. Study of the literature and personal observations prove that in the question about the effect of meals and nutrition on the functional

status of the higher sectors of the central nervous system, some concepts must be distinguished. First of all, in the function of the higher sectors of the central nervous system, we should differentiate changes which arise during and immediately after eating, from changes which develop under the effect of a long, continued consumption of these of other food substances. In the first case, the changes develop quickly, and they last for a comparatively short time (1-3 hours), while in the second case, the chances develop slowly, but are more permanent. It should be kept in view that one and the same food substance, or one and the same food regime, may cause different, sometimes even diametrically opposite changes. For instance, after its prolonged consumption, carbohydrate food will lead to lowering the excitability of brain and to a diminution of conditioned and unconditioned reflexes. At the same time, the carbohydrate rood regime, which is prescribed after a mixed nutrition, provokes a rise of the excitability process (G. YU. GRINBERG, 1928; V. S. MUZYKANTOV, 1933). Usually, man eats a mixed food. It is not amazing that, after the intake of easily soluble carbohydrates(sugar, confectionaries), each time we noticed a considerable increase in the excitability of the brain.

For the solution of the question about the qualitative characteristics of nutrition for nightworkers, the most important is, in the final analysis, to consider the shifts which develop in the function of the central nervous system under the influence of eating itself. Above, we showed that, after the intake of the majority of food substances (milk, kefir, cottage cheese, bread, bacon, small sausage), the higher sectors of the central nervous system answer with a signal-type reaction, judging from the findings of optical adequate chronaxia: -- after a brief period of excitement for the length of 10-15 min., a very long period follows, char-acterized by lowered excitability. These changes ought to be considered as manifestations of the general biological law, proper, in some degree, to the whole living world. The biological meaning of this phenomenon is fully understandable: -- a reduction of the excitability of the higher sectors of the central nervous system results in an increase in the irritability of the subcortex, by which favorable conditions are created for the course of the digestive process. It is characteristic that the greater the stress by which the food is digested in the gastro-intestinal tract, the greater the degree by which after the food intake, the brain excitability is lowered. We do not find any other explanation for the results of investigations where, under identical conditions, the intake of bacon causes more distinct lowering of the cerebral excitability than small sausages, while among dairy products, cream and cottage cheese cause more distinct lowering than whole milk. A large mass of charming observations

could be brought up when, after an abundant meal, somnolence, and even sleep develops in animals. N. VOLFSON (1961) mentions one of them.

During work on the film, "Striped Voyage," a picture had to be taken in which a lion enters a passenger cabin, climbs on the sofa, and falls asleep. KONSTANTINOVSKIY, the tamer, abandoned the service of veterinary physicians who suggested to put the lion asleep with the aid of hypnotic drugs, and he found another, more natural way. Before picture taking, he gave the lion 20 kg meat instead of 7 kg. The greedy lion ate up all the meat, and soon he fell asleep. When the camera started working, the lion opened only one eye, for listening. But the natural need of sleep after a substantial dinner did its best, and he fell asleep, even started to snore.

Thus, after food taking, especially after eating substantially, after the consumption of hardly digestible products, the excitability of the brain is lowered. As our investigations showed, the cerebral excitability drops particularly markedly after the taking of food in the evening and night hours. In the evening hours, the excitability of the brain drops, not only after a copious meal, but also after a very moderate, even light supper. This proves once again that in the evening , in the central nervous system, there is an increased readiness for the development of inhibitory processes. By the way! Let us remark that this physiological method can be utilized for the normalization of sleep in insomnia connected with disorders in the period of falling asleep.

From the quoted facts. a very important rule follows for the construction of nutrition for nightworkers. Since, in t the evening and night hours under natural physiological conditions, a drop is observed in the cerebral excitability, then this condition should not be redoubled by the food intake. The diet should be composed from such products after whose intake, the cerebral excitability not only would not be lowered but, on the contrary, it would have a tendency to rise. Unfortunately, we have at our disposal, only a very small number of food substances whose intake is accompanied by a distinct rise in brain's excitability. These are, chiefly, the easisly soluble carbohydrates (sugar, chocolate, cocoa, coffee and tea). From among other food substances, the taking of milk and milk products goes with a lesser drop in cerebral excitability. Evidently, from these products, the ration should be made up for nightworkers.

Starting from the ideas of I. M. SECHENOV on the mutual relationship between the higher neural centers and the periphery in the process of working operation, a high producti-

vity of work, in particular muscular working capacity, can be reached only with a high working capacity of the cells of the higher sectors of the central nervous system. We have also found this at the study of the methods of raising muscular working capacity at night. It was shown that muscular working capacity increased at night, and rises distinctly, and comparatively promptly, after the intake of certain foods which raise cerebral excitability. According to the data of our research, such foods proved to be vitamin-enriched chocolate. It seemed to us that these investigations are important from a fundamental point of view, but not from the point of view of practical recommendation. It is important that, with the aid of food substances, human working capacity can be raised at night. As to the utilization of chocolate for these purposes, this is not without a practical interest, in particular chocolate can be recommended to pilots during night flights, and to other specialists whose activity is connected during night operations with a high psycho-neural stress.

The effort at increasing the functional activity of the higher sectors of the central nervous system in nightworkers was made, not only by a desire for the imporvement of work productivity, but also by the need to prevent the development of pathological conditions.

As it is well known, one of the most harmful effects on the central nervous system is considered, by I. P. PAVLOV, the simultaneous of chronologically close employment of stimuli which provoke excitation and inhibition---this is the so-called collision. After some time, such an effect disturbs the normal course of neural processes, and provokes the development of pathological states in higher neural functions.

At night, in the function of the central nervous system, a tendency is noticed toward inhibitory processes, toward the lowering of cerebral excitability, and if there are no hindering factors, then sleep will develop. However, the working activity is usually connected with the activation of a stimulating process, with the creation of stimulation foci in the higher sectors of the central nervous system. Thus, in the process of night work in the activity of the higher sectors of the central nervous system, two opposite tendencies appear simultaneously: one directed at lowering, and the other at increasing the excitability of the brain. A situation is created which can lead to the development of pathological conditions. There is nothing surprising in the fact that many investigators observed the development of a neurosis in experimental animals when the circadian tide was disturbed and the diurnal routine was altered (G. M. CHERKOVICH, 1961).

-31-

Our findings indicate that, with certain therapeutic measures, though no normalization can be obtained in hypertensive patients, in every case a smoothening of the perversion of the circadian tide of vegetative functions can be obtained.

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Thus, we used a daily oxygen therapy session to establish that the circadian variation conclude pressure is reduced in hypertensive patients, and under the same conditions their gaseous metabolism is improved.

The character of the action of medicinal substances is also distinctly dependent on the circadian periodicity of physiological functions. With a comparative employment of nitrites in hypertensive patients in daytime and at night, our investigations showed that, under the influence of nitroglycerin, more marked hemodynamic changes develop in hypertensive patients at night than in the daytime.

The influence of a single intake of the usual therapeutic dose of nitroglycerin causes a more marked reduction of the systolic and minute volume of the blood, a lowering of the tonus of muscular arteries and arterioles, a lowering of all blood pressure indices, and a more marked acceleration of the heart beat in hypertensive patients at night than during the daytime. These features of nitroglycerin activity at night are much less marked in patients who are in later stages of the ailment than in patients who are in the initial stages. Studying the large incidence of anginal attacks at night in hypertensive patients, we should keep in view the mentioned characteristice of hemodynamic changes when prescribing nitrites for such patients.

We are far from the idea to consider our investigations into the study of the circadian tide of vegetative functions in health and disease completed. Further investigations along the same line are unquestionably very promising.

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-32-

# TABLE OF CONTENTS

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Introduction	3
CHAPTER I. Hole of the diurnal periodicity of physiolo- gical functions in the vital activity of the or- ganims, and contemporary ideas on the nature of sleep	7
CHAPTER IL Functional status of the higher departments of the central nervous system	20
Diurnal fluctuation Diurnal fluctuation of the excitability of higher departments of the central nervous	
 system in healthy and sick persons Changes in the functional status of the higher departments of the central nervous system caused	22
by food intake Fitness for muscular work and energy losses at an	25
apportioned physical job	32
CHAPTER III. Functional state of the system of blood circulation	36
nightwork Hemodynamics in hypertensive persons Peculiarities in the effect of vasodilators (ni-	44
trites) at night in hypertensive persons Hemodynamics in peptic ulcer patients (gastric and	56
duodenal) Circadian periodicity of electrocardiographic	61
CHARTER THE Dubmonary wontilation and are evoluted	67 70
Charles iv. Fulmonary ventilation and gas exchange	70
CHAPTER V. Functional status of the digestive system Functional state of the salivary glands	75
Secretory function of the stomach in the hours of night outside the digestive	83
periodQualitative marks of supper, and the noc-	
turnal gastric secretion	93
Gastric digestion during sleep Analysis of the composite reflex and neuro-humoral phase of gastric secre-	99
tion	100

٠

Activity of digesting dairy food during sleep	104
gestion (experimental investigation)	107
mach in sleep	110
Functional condition of the hepato-pancreatico- duodenal system	114
side the digestive period	
secretory function of the hepato-pancre- atico-duodenal system in sleep Functional state of the liver Carbohydrate function Synthetizing function Deamination and urea-forming func-	122 125 126 129
tion	13±
Digestive leukocytosis and specific dynamic effect of food in healthy persons at night	135
CHAPTER VI. Sleep disorders and some means of its nor- malization Methods of extimation sleep dynamics	142 
gans	147
Effect of the act of eating and digesting upon the depth of sleep A few methods of sleep normalization	154 157
CONCLUSIONS (results and prospects of future investiga- tions)	160
LITERATURE	186

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•

-34-

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