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Change in Serotonin Level in the Organism in Cases of Hypoxia

T. Sachanska, Ph.D., D.Sc.

National Center of Hygiene, Medical Ecology and Nutrition, Sofia, Bulgaria

Abstract: This study was performed on both volunteers and test animals subjected to different extreme effects, causing different types of hypoxia. It is found that at high initial values of blood serotonin, the organism is more resistant to hypoxia. In individuals in whom the serotonin level is increased after extreme impacts, the hypoxic state is less readily sustained. The results of this study are used for determining the individual reactivity of an organism to hypoxia and for selecting for hire persons who may be required to work in extreme conditions.

Hypoxia is one of the main events after organism injury in extreme conditions and in certain diseases of the cardiovascular, nervous, and respiratory systems [1–4]. It has been established that hypoxia is an important sequela in hyperbaric, hypobaric, and hypergravitational impacts, intoxications, and other extreme physiological situations. In contrast, hypoxia is the cause of overloading of the adaptive regulatory mechanisms of the organism. Studies on the pathogenesis of hypoxia have determined the significant role of the vasoactive biogenic amines, including serotonin, as regulators of cerebral blood flow.

The objective of the work reported herein was to study the dynamics of blood serotonin changes in order to clarify the role of this vasoactive amine in the pathogenesis of different types of hypoxia. The results of such studies are significant for clarifying the problem of resistance of an organism to hypoxia in various extreme conditions, which is particularly important for the professional selection of people who may be required to work under such conditions, as well as for health risk assessment and design of prophylactic and treatment regimens.

MATERIALS AND METHODS

Investigations of serotonin in blood in 288 volunteers and 159 experimental animals were performed in the condition of extreme impact and in 293 patients with different forms of hypoxia. According to the classification of hypoxia adopted by the author and his colleagues, the experimental material is distributed as follows:

General hypoxia,

Altitude hypoxia: modeled by hypobarism in 53 volunteers and 31 experimental animals,

Circulatory hypoxia: modeled by hypergravitation and hyperbarism in 35 volunteers and 102 experimental animals,

Circulatory hypoxia in patients with hypotension: 127 children,

Local hypoxia,

Local cerebral hypoxia in vascular diseases: 98 patients with vascular headache and 68 patients with pathological processes of the main cerebral vessels,

Model of local hypoxia by ligature of the vertebral artery: 20 experimental animals,

Isolated hypoxia of the labyrinth: 96 experimental animals with labyrinthectomy,

Toxic hypoxia: 10 experimental animals treated with BZ and 10 experimental animals treated with BZ and antidote KK-4.

Hypoxia generally is determined by clinical and electrophysiological investigations, though in animals and patients with stroke, morphological investigations are employed.

Blood samples for studying serotonin are collected 24 hours (volunteers) and 30 minutes (experimental animals) before the extreme impact and 15 minutes after its end. Serotonin is studied by the spectrofluorometric

Reprint requests: T. Sachanska, Ph.D., D.Sc., National Center of Hygiene, Medical Ecology and Nutrition, 15 Dimiter Nestorov Street 1431, Sofia, Bulgaria.

method devised by Snyder et al. [5] and modified by Kulikovskii and Kostjukovskaja [6] and Sachanska [7].

The experiments on test animals enable monitoring of the dynamics of biochemical, electrophysiological, and clinical changes and comparison of these data to the morphological findings. In addition, morphological verification can be performed at each stage of the hypoxic effect.

Serotonin has vasoconstrictive and hormonal effects (so-called stress hormone). Its values depend on the season of the experiment; on the age and type of subjects studied; and on the character, intensity, and duration of the extreme impact, among other factors. It has been established that the standard serotonin values in humans and different animal species vary widely [6]. This variation is aggravated particularly in the setting of extreme impacts. For this reason, we use autocontrol (study of the same subject before and after impact) to ensure reliability of the obtained results. Owing to the variability in serotonin values, we distributed the studied subjects among three groups: (1) low serotonin values; (2) medium serotonin values; and (3) high serotonin values.

The development of adequate experimental models of different types of hypoxia that will enable us to conduct complex medicobiological studies was one of our main goals. Hence, we include in this report a description of the particular experimental models, which allows complex presentation of the various types of hypoxia, results of our examinations, and discussion on the obtained data.

RESULTS AND DISCUSSION

General Hypoxia

Altitude Hypoxia

In a hypobaric chamber, altitude hypoxia is modeled by decompression of a simulated elevation of altitude. The investigations were performed under the conditions of moderate and acute degrees of hypoxia. A moderate degree of hypoxia was achieved by steplike elevation of altitude to 5,500 m; the cadets remain on the site for 30 minutes and the animals 45 minutes. An acute degree of hypoxia was tested in animals only, by steplike elevation of altitude to 10,000 m, the stay at each site being 5–10 minutes for adaptation to the particular altitude.

As evidenced in Table 1, the background serotonin values in all candidate cadets are significantly higher than the respective values in professional pilots and student pilots. This probably is due to the strong neuropsychic stress on study participants before the examinations and of the uncertainty of hypobaric loading. The candidate cadets of the third group, in whom serotonin values decrease after hypobaric loading, are more stable to hypoxic effects. This is confirmed by the results of the clinical and electrophysiological investigations.

Table 2 presents the serotonin values for experimental animals. A moderate degree of hypoxia is tolerated comparatively well by all animals, and they survive without visible symptoms of cerebral hypoxia or decompression disease. Acute hypoxia is modeled only in test animals by stepwise elevation to 10,000 m. As already noted, the animals' stay at each stage is 5–10 minutes: The duration of stay on a particular altitude site is determined individually depending on the electrophysiological data (pulse rate, electrocardiogram [ECG], electroencephalogram [EEG]), which point to the proceedings of the adaptation processes and current state of the organism.

Table 3 displays the results of serotonin determination in animals subjected to acute hypoxic impact. The acute form of hypoxia confers significant stress on the organism. The electrophysiological data show that initial tachycardia is replaced by severe bradycardia. Sharp disturbances in cardiovascular activity occur, manifested by arrhythmia, extrasystoles, and an impaired QRS complex configuration. Respiration is accelerated and surface. EEG activity disappears gradually, and flat curves are observed. Heart activity stops, and some animals die (57%). Comparison of the two experiments shows that the animals with high initial values of serotonin are significantly steadier in the face of hypoxic effect relative to those subjects with lower or average background serotonin values.

General Circulatory Hypoxia

Circulatory Hypoxia at Hypergravitation. Circulatory hypoxia at hypergravitation is modeled in a centrifuge for pilot training, using an arm length of 720 cm. The air-fight scenario is used, with variable accelerations: 4, 5, and 6 +Gz over 180 seconds, the gradient of acceleration increase being 0.2–1.0 +Gz, with background cycle values of 3 +Gz. For cadet pilots, the cycle is repeated three times and, for test animals, four times. The rest between the cycles is 1 minute.

The animals are placed in the cockpit in special cages, the loading vector acting in craniocaudal direction (head-pelvic girdle).

Hypoxia occurs during hypergravitational impacts owing to the redistribution of blood, which is redirected to lower (hind) limbs. In addition, vestibular dysfunction occurs owing to the gravitational overloading of the vestibular analyzer, particularly its otolith part.

Table 4 indicates that in cadets from the first group, there is a significant increase in blood serotonin concen-

Table 1. Changes in Serotonin Values in Cadets After Hypobaric Impact (5,500 m with 30-minute stay on the ground)

	Before impact			After impact				
Serotonin	**n**	$\bar{x}$	$S\bar{x}$	**n**	$\bar{x}$	$S\bar{x}$	*t*	*p*
First group (≤1,962 nmol/liter)	16	1,387	108	16	2,239	234	3.291	<.01
Second group (1,963–3,412 nmol/liter)	20	2,653	82	20	3,349	269	2.466	<.02
Third group (>3,413 nmol/liter)	12	4,664	383	12	4,071	381	1.093	>.05

trations after hypergravitational impact; in cadets of group 2, the increase is insignificant; and in group 3 cadets with high initial values of serotonin, the serotonin concentration decreased. It should be noted that during hypergravitational stress, the cadets from group 1 and some from group 2 exhibit significant changes in the ECG and EEG (see the column, "Tolerance"). They record extrasystole as bigemina and trigemina, and sometimes as black or gray curtain, indicating a near-collapse. The cadets from group 3 demonstrate increased resistance to hypoxia, as confirmed by clinical and electrophysiological examinations, indicating that persons with high background serotonin values are significantly more resistant to hypergravitational hypoxia.

Table 5 presents the data of serotonin studies in animals subjected to hypergravitational loading. The rabbits from groups 1 and 2 experienced increased serotonin concentration after leaving the centrifuge. During the hypergravitational impact, initial tachycardia that progresses to severe bradycardia, the appearance of extrasystoles, and ECG changes were recorded in these subjects. Some of the animals (33%) could not survive the stress and died.

Rabbits with initially high background values experienced decreased blood serotonin and were more resistant to hypoxic impact. Rabbits subjected to hypergravitational stress sustained it with less ease than they did hypobaric impact. Repeated centrifuging after 48 hours rest was sustained with particular difficulty.

Circulatory Hypoxia at Hyperbaric Conditions. The investigations for modeling common circulatory hypoxia under hyperbaric conditions were performed in one of two types of hyperbaric chambers: a small bisector barochamber, in which the pressure increases up to 11 ATA (100-m imitated depth), and a large bisector barochamber for saturation diving, in which the pressure can be increased to more than 11 ATA. Divers can live in this chamber from 10–12 days to 1 month at increased pressure.

Short-term and long-term hyperbaric effects were measured. At hyperbaric impacts and inadequate compression and decompression modes, a gas embolus often formed in the organism before the balance was set between the pressure in the chamber and the pressure of the gases in the organism itself (i.e., balance between saturation and desaturation processes). In these cases, circulatory hypoxia occurred due to obstruction of the vessels by gas embolus.

Table 6 displays the changes in serotonin values in divers at hyperbaric stress of 8.5 ATA (75-m depth) in an air environment with a 20-minute stay on the ground. It reveals that the serotonin values were mainly increased, decreasing in only one diver. The data from clinical and electrophysiological examinations evidence this diver's better adaptation ability and resistance to hypoxic factor.

So-called saturation diving is popular nowadays (i.e., hyperbaric impacts related to a prolonged stay on the ground). After the saturation processes are completed, the diver can work in this state for a long time (hours to days) in increased pressure. Decompression is performed once at the end of the work but for an extended time depending on the depth at which the diver was working. Table 7 presents the results of blood serotonin studies in divers participating in saturation diving to 4 ATA (30 m), 11 ATA (100 m), and 21 ATA (200 m) in a triple-gas (helium-oxygen-nitrogen) breathing environment.

With the application of a nonnatural breathing environment, there is always risk of insufficient homogenization of the components and formation of "helium

Table 2. Changes in Serotonin Values in Rabbits After Moderate Hypobaric Impact (5,500 m with 45-minute stay on the ground)

	Before impact			After impact				
Serotonin	**n**	$\bar{x}$	$S\bar{x}$	**n**	$\bar{x}$	$S\bar{x}$	*t*	*p*
First group (≤1,788 nmol/liter)	3	1,420	172	3	4,889	1,098	3.12	<.05
Second group (1,789–2,768 nmol/liter)	3	2,203	260	3	2,108	346	0.291	>.05
Third group (>2,769 nmol/liter)	2	3,943	482	2	1,248	57	5.558	<.05

Table 3. Changes in Serotonin Values in Rabbits After Acute Hypobaric Impact (10,000 m with 10-minute stay on the ground)

	Before impact			After impact				
Serotonin	**n**	$\bar{x}$	$S\bar{x}$	**n**	$\bar{x}$	$S\bar{x}$	*t*	*p*
First group (≤1,788 nmol/liter)	2	621	20	2 (2 ex)	1,836	1,160	1.07	>.05
Second group (1,789–2,768 nmol/liter)	5	2,348	88	5 (2 ex)	3,489	228	4.66	<.002
Third group (>2,769 nmol/liter)	5	3,358	227	5	2,104	375	2.86	<.025

clouds." During our studies, one of the divers got in such a cloud and had an episeizure due to the severe cerebral hypoxia.

The results from serotonin studies (see Table 7) show that at 4, 11, and 21 ATA in the prestart period, serotonin levels increased in all divers as compared to the background period. This is a reflection of prestart tension and recognized risk. The serotonin values 30 minutes after decompression indicate a slight decrease. At greater depths—11 and 21 ATA—in the postdecompression period, significant additional increases of serotonin were recorded, probably indicating overstress of the serotoninergic system during the entire stay in an increased-pressure and nonnatural gas environment.

These data illustrate that the determination of serotonin levels can serve as a prognostic aid regarding the reactivity of an organism to hyperbaric loading and professional selection of divers for actual saturation diving. The serotonin data together with the complex of electrophysiological, clinical, and psychophysiological examinations allowed us to make a preliminary selection of and prognosis for the individual stability of candidates for true saturation diving. These prognoses were confirmed by the test saturation hyperbaric loadings at 11 and 21 ATA.

The test divings (i.e., hyperbaric loading in a barochamber) always were preceded by experiments with animals. Rabbits, guinea pigs, cats, and goats were subjected to similar impacts, in an effort to determine the animals' individual resistance to circulatory hypoxia. Table 8 shows the results of serotonin investigations in rabbits subjected to hyperbaric loading at 8.5 ATA with a 20-minute stay on the ground and a decompression mode selected according to tables designed for each animal species.

After hyperbaric impact, the animals with low values of serotonin (group 1) are significantly unsteady and, during hyperbaric loading, some of them die. The development of decompression disease was confirmed after decapitation: Numerous gas emboli were evident in the vessels, organs, brain, omentum, and fat tissue, accompanied by ischemic foci and hemorrhages in the brain and internal organs. The blood serotonin concentration after hypoxic impact was increased insignificantly in the rabbits from group 2, whereas the animals from group 3 proved to be significantly more resistant to barochamber loadings and did not manifest visible clinical symptoms of decompression disease.

Goats and guinea pigs sustained the hyperbaric loading significantly better as compared to cats and rabbits. The results of these serotonin studies in circulatory hypoxia can be generalized thus: Humans and animals with high background serotonin values experience decreased serotonin levels after hyperbaric impact and are significantly resistant to the hypoxic factor. This generalization suggests that serotonin investigations might be used effectively in the professional selection of divers, particularly those who are being prepared for deep diving.

General Circulatory Hypoxia in Patients with Hypotension

Primary arterial hypotension has long been considered a favorable state that prolongs life. Recently, much consideration has been given to this state's many unfavorable effects on the organism due to the existing general hypoxia in the organism. Bearing in mind these data, we studied the concentrations of serotonin in the blood of children suffering from hypotension, who were distributed into two groups: In the first group

Table 4. Changes in Serotonin Values in Cadets After Hypergravitational Impact According Air-Fight Scenario

	Before impact			After impact					
Group	**n**	$\bar{x}$	$S\bar{x}$	**n**	$\bar{x}$	$S\bar{x}$	*t*	*p*	**Tolerance to +Gz**
First group (≤513 nmol/liter)	5	404	39	5	618	78	2.45	<.05	Extrasystoles as bigemina or trigemina, "black curtain"
Second group (514–632 nmol/liter)	8	595	42	8	601	136	0.13	>.05	Extrasystoles as "gray curtain"
Third group (>633 nmol/liter)	12	950	74	12	700	53	2.72	<.025	Good tolerance

Table 5. Changes in Serotonin Values in Rabbits After Hypergravitational Impact in a Centrifuge at Air-Fight Scenario

	Before impact			After impact				
Serotonin	**n**	$\bar{x}$	$S\bar{x}$	**n**	$\bar{x}$	$S\bar{x}$	*t*	*p*
First group	3	1,297	234	3 (2 ex)	2,343	623	1.571	>.05
Second group	6	2,359	138	6 (1 ex)	2,610	598	0.408	>.05
Third group	4	4,145	252	4	2,333	381	3.986	<.01

were children aged 6–9 years (17 girls, 20 boys), and in the second group were children aged 10–15 years (43 girls, 47 boys). It was established that in the first group no statistically significant gender-dependent differences in serotonin levels existed (average values: girls, 974 nmol/liter; boys, 827 nmol/liter). In the teenage period, however, the values of serotonin were significantly higher than in the first group (average values: girls, 1,155 nmol/liter; boys, 1,725 nmol/liter). The differences were statistically significant both regarding the genders in the two groups and the age of the subjects in the two groups. These results are preliminary.

Local Hypoxia

Local Cerebral Hypoxia in Vascular Diseases

Patients with Migraine. Vascular headache is one of the most frequently encountered reasons for discomfort and diminished work capacity. The etiology and pathogenesis of this disease are not completely understood and, therefore, treatment is not sufficiently effective.

Data about the role of serotonin in migraine are controversial. Some authors make a distinction between migraine and grapelike (blast) headache, suggesting that the blood serotonin values determine the clinical picture and treatment. Blood serotonin levels usually are elevated during migraine headaches.

Examination of 85 patients with migraine and 13 patients with blast headache was conducted. Blood samples were collected from the majority of them during a crisis and in the period between crises. It was established from the studies of serotonin that individual differences exist: Some patients (57%) experienced serotonin during crisis, though the changes are statistically insignificant in some. In a single case during crisis, the serotonin level was decreased from 520 to 471 nmol/liter.

Noteworthy is the case of one patient with blast headache in whom, in the period between crises, the serotonin concentration was 2,838 nmol/liter (normal, 397–539 nmol/liter). After antiserotonin treatment, the patient's state improved and the serotonin values normalized. The blast headache disappeared for 3 years. After a psychic trauma, the patient developed transitory paresis, which disappeared after 3–4 days. Several days later, the patient suddenly developed coma and died in 6 hours. The pathoanatomical examination showed massive cerebral hemorrhage invading the ventricles and the subarachnoid space.

Another patient with migraine had increased serotonin values in the period between crises (946 nmol/liter) which, during a crisis, were elevated even further (2,780 nmol/liter, or a 294% increase).

These results show that there are individual differences in blood serotonin values both between and during crises. These differences in the serotoninergic system have not yet been studied adequately.

Patients with Stenosis and Thrombosis of the Main Cerebral Vessels. In the case of pathological changes of the main cerebral vessels, focal brain ischemia can be combined with hemorrhages. In addition, in the presence of hemorrhagic insults and subarachnoid hemorrhage, ischemic foci are observed around the hemorrhages due to spasm of the cerebral arteries. This spasm is provoked by excretion of serotonin (a strong vasoconstrictor) from the lacerated vessel.

Table 6. Changes in Serotonin Values in Divers After Hyperbaric Impact of 8.5 ATA with a 20-Minute Stay on the Ground in Air Environment

	Before impact			After impact				
Serotonin	**n**	$\bar{x}$	$S\bar{x}$	**n**	$\bar{x}$	$S\bar{x}$	*t*	*p*
First group (≤513 nmol/liter)	4	422	28	4	459	23	1.233	>.05
Second group	10	592	19	10	643	54	0.943	>.05
Third group	1	839		1	527			

Table 7. Changes in Serotonin Values in Divers at Saturation Diving

Initial pressure	Background	Before saturation diving	30 minutes after decompression	72 hours after decompression
4 ATA				
RK	556	703	680	—
GG	487	864	763	—
11 ATA				
SS	412	634	836	—
BW	414	539	565	—
NK	675	1,480	2,831	—
21 ATA				
SS	441	668	1,141	882
NK	791	912	1,430	973
DZ	373	943	1,521	456

Clinical, electrophysiological, x-ray, and biochemical examinations were conducted in 68 patients with hemorrhagic insult (n = 34), subarachnoid hemorrhage (n = 21), and ischemic insult (n = 13). Cerebral hemorrhages prevailed in patients with moderate and low blood serotonin values. We could not draw any conclusions as we lack sufficient data on the dynamics of serotonin changes in the different stages of the disease.

Increased serotonin values were observed in 70% of the cases of subarachnoid hemorrhage (average, 766 nmol/liter). In the other 30% of cases, serotonin was normal or lower (< 272 nmol/liter). Increased serotonin values (up to 3,688 nmol/liter) prevailed in cases of ischemic (thrombotic and nonthrombotic) insults. A good prognosis coincided with rapid return of the serotonin level to normal values, but cerebral vessel disease can lead to death if these levels remain high during several days.

The determination of serotonin levels is valuable for the diagnosis and prognosis of cerebral vessel disease in the cases of subarachnoid hemorrhage, hemorrhagic insult and, to a lesser degree, ischemic insult. In the latter cases, it is necessary to monitor the blood serotonin dynamic, as a single examination of serotonin level is insufficient.

The results of these investigations show that at increased concentrations of serotonin in blood (particularly very high values [i.e., two to three times the reference values]), the prognosis for stenosis or thrombosis of cerebral vessels is not favorable.

Local Cerebral Hypoxia in Animals by Ligature of the Vertebral Artery

Cats were used as an experimental model for observing the effects of extracranial and intracranial ligature of the vertebral artery. The ligature was performed by extracranial clipping of the artery (silver clips) at level C-1 (10 animals) and intracranial clipping of the fossa cranii posterior (10 animals). Blood samples for studying serotonin were collected before and 60 and 120 minutes after the clipping. Brainstem evoked potentials, auditory and visual evoked potentials, and microphone and action auditory potentials before the obstruction and during the experiment were recorded. The results are presented in Table 9.

A statistically significant increase of the serotonin concentration in blood was observed 60 minutes after clipping, at which time the cochlear microphone and action potentials (decreasing amplitude) revealed the development of severe hypoxia of the labyrinth. Similar changes were observed in the brainstem potentials, visual evoked potentials, ECG, and respiration. These findings indicate the development of hypoxia in the entire vertebrobasilar system.

At 120 minutes, some decrease in the serotonin values was established, but these remained significantly

Table 8. Changes in Serotonin Values in Rabbits After Hyperbaric Impact of 8.5 ATA with a 20-Minute Stay on the Ground and Normal Decompression Mode

	Before impact			After impact				
Serotonin	n	$\bar{x}$	$S\bar{x}$	n	$\bar{x}$	$S\bar{x}$	*t*	*p*
First group (≤1,788 nmol/liter)	14	1,378	52	14 (4 ex)	2,473	397	22.735	<.025
Second group (1,789–3,412 nmol/liter)	11	2,296	74	11	2,214	271	0.291	>.05
Third group (>3,413 nmol/liter)	12	3,764	208	12	2,036	283	4.915	<.01

Table 9. Changes in Serotonin Values in Cats After Ligature of Vertebral Artery

	n	$\bar{x}$	$S\bar{x}$	*p*
Before ligarure	10	412	147	
60 minutes after ligature	10	752	231	<.001
120 minutes after ligature	10	539	220	>.05

Table 10. Changes in Blood Serotonin Values in Guinea Pigs After Unilateral Labyrinth Destruction

	n	x	$S\bar{x}$	*t* on/k	*p*
Experimental group	8	320	37.3		
Control group	3	414	22.8	2.82	<.025
Narcosis control	3	408	23.7	0.10	>.05

higher than the initial levels ($p < .05$). The electrophysiological and microscopical examinations showed that this is the period during which the collateral circulation of the brainstem and labyrinth is engaged.

Isolated Hypoxia of the Labyrinth

Working environments that are characterized by noise, vibrations, high velocities, and accelerations having parameters that exceed the hygienic admissible standards are known to lead to dysfunction of the auditory-vestibular system. Such problems are reported with increasing frequency. The pathogenesis of these disturbances, the degree of involvement of the different compartments of the vestibular analyzer, and the mechanisms of compensation of vestibular-sensor and vestibular-vegetative somatic disturbances have not yet been studied sufficiently.

Believing that the realization of an experimental model of vestibular dysfunction might shed some light on these issues, we invoked an experimental model of vestibular dysfunction in 84 guinea pigs, 7 cats, and 5 rabbits. Right-ear labyrinthectomy was performed by a mechanical-chemical method according to Emilyanov and Alexin [8] (modified by Daneshka). The animals were under urethane narcosis (400 mg/kg). A narcosis control group also was used in which the animals were treated only with urethane (400 mg/kg). Blood samples for studying serotonin were collected 96 hours after intervention when, according to morphological data, full destruction of the labyrinth had already occurred.

Table 10 shows that 96 hours after labyrinthectomy, the blood serotonin values were significantly decreased ($p < .025$). The comparison of data of both control groups indicate that narcosis does not influence blood serotonin concentration ($p > .05$).

The electrophysiological data show that immediately after the intervention, EEG desynchronization, tachycardia, and rhythm deviations occur and, after 27–38 minutes, nystagmus and specific motion disturbances appear. Morphological examination demonstrated a bulla full of a colorless, structureless matter and a fully degraded cochlea 72 hours after the intervention. These results could be used when studying the pathogenesis of auditory-vestibular and vestibular-vegetative disturbances and their compensation mechanisms.

Toxic Hypoxia

BZ in humans and animals causes toxic cerebral hypoxia, as evidenced during the war in Vietnam. The effect of psychosomimetic substance BZ was studied on 64 guinea pigs and 30 cats. The serotonin concentration in the blood of the experimental animals was studied before and after administration of BZ and after applying the antidote (KK-4). During the experiment, the electrophysiological indices characterized the central nervous system and cardiovascular system activities.

Table 11 shows that after administration of BZ, the serotonin concentration in blood decreased and, after administration of the antidote KK-4, its concentration increased. As a result of serotonin evaluations and investigation of some electrophysiological parameters, the effectiveness of antidote KK-4 was established. A complex of medicobiological examinations has shown the effectiveness of the administered antidotes and identified the most appropriate dosage.

Serotonin investigations are particularly important in cases of intoxication with psychosomimetic substances and at application of psychotropic preparations. Monitoring of blood serotonin concentration dynamics is significant for controlling treatment.

It is considered that the application of psychosomimetic substances in animals is a suitable model of schizophrenia, because intoxication with LSD-25 and BZ in humans provokes a picture similar to that of schizophrenia. Wooley [10–11] theorizes that schizophrenia appears in some cases after serotonin deficit, whereas hallucinations are not always related to such a deficit.

CONCLUSIONS

By monitoring serotonin changes while studying various types of general and local hypoxia, we have shown that the serotoninergic system plays a significant role in the development of the processes of general and specific adaptation, readaptation, and compensation. These studies are of particular importance for professional selection of persons whose employment might expose them to special conditions such as hypobarism, hyperbarism, and hypergravitational impacts. They are im-

Table 11. Changes in Serotonin Values in Cats After Intoxication with BZ and Administration of Antidote KK-4

N	Background	30 min after BZ	Deviation (%)	30 min after KK-4	Deviation of KK-4 (%) versus Background	Deviation of KK-4 (%) versus BZ
18	1,349	939	−41	—	—	—
21	1,525	469	−70	—	—	—
23	1,173	762	−35	—	—	—
24	1,056	880	−17	—	—	—
1	2,259	2,787	+23	2,875	+28	+3
2	1,203	1,173	−19	1,261	+5	+8
3	1,467	264	−82	733	−50	+178
4	1,408	1,232	−13	1,760	+25	+43
5	—	1,584	—	1,877	—	+18
6	587	880	−7	1,467	+150	+67
	2,934	2,757	−17	3,168	+8	+15

portant also in determining prophylactic therapy and treatment of patients affected by hypoxic injury.

The relation between extreme impact and response of the organism (as a whole or of its systems) is very complex. Highly significant is the role of individual reactivity, which is the result of the interaction of many factors, most of which are still incompletely understood. High initial values of blood serotonin are related to increased resistance of the organism to different hypoxic impacts. The tolerance to hypoxia is a critical characteristic for such professionals as pilots, alpine climbers, and cosmonauts.

The results of these investigations lead to the following important conclusion: Investigation of serotonin levels, and particularly the monitoring of its dynamics, is extremely important not only for the professional selection of workers who will be exposed to extreme hypoxic conditions but also for the diagnosis and treatment of and prophylactic therapy for certain vascular, neurological, and psychic diseases.

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