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MECHANISM OF AN ACUTE INCREASE OF INTRACRANIAL PRESSURE AND ITS HARMFUL INFLUENCE ON BRAIN TISSUE

This article is a reprint of a previously published chapter of a monograph by Atchabarov Bahiya "Synopsis of Physiology and Pathophysiology of cerebrospinal fluid dynamics and Intracranial Pressure", Gylym, 1996, pp. 201-226 (in Russian).

A monograph published in 1996 is a summary of the author and his colleagues' previously published studies on the intracranial pressure in normal and pathological conditions. The monograph describes various causative factors for intracranial hypertension such as cerebrospinal fluid disturbances, brain swelling, changes in blood supply in the craniospinal cavity, and the consequences of changes in blood pressure. The physiology and pathophysiology of cerebrospinal fluid dynamics (cerebrospinal fluid production, circulation and resorption) have also been studied. The monograph analyzes and explores previously known and obtained in many years of research own scientific data.

Keywords: *intracranial pressure, acute brain herniation, cerebrospinal fluid dynamics.*

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Abbreviations

ABH – acute brain herniation
ABT – acute brain trauma
AP – systemic arterial pressure
CFP – cerebrospinal fluid pressure
CrE – indicator of the blood supply of the brain, determined by the method of injection of the labeled (Cr-51) erythrocytes
CSC – craniospinal cavity
CSF – cerebrospinal fluid
CSS – craniospinal system
DR – dry residue of the brain
FP – filtrating pressure
G – standard deviation of the M
ICP – intracranial pressure
IOP – intraocular pressure
IR – integral rheogram
IRH – integral rheogram of the head
IVP – intracranial venous pressure
M – mean value
M±m – mean value of an indicator with its error
PB – ICP or CSF pressure at baseline, i.e. ICP (true, i.e. actual) prior to measuring PR or PP (ICP or CSF pressure)
PC – penetrance coefficient
PP – new maximum CSF pressure (ICP) level after additional volume (ΔV) is introduced into the subarachnoid cavity, mmH2O
PR – CSF pressure (ICP) level measured by an L-shaped glass pressure gauge; residual CSF pressure after extracting part ("excess" volume - ΔV) of the cerebrospinal fluid from the subarachnoid cavity, mmH2O
q = ΔP/ΔV – coefficient of the rigidity of the craniospinal cavity
ΔP – difference between PB and PR, or PP and PB
ΔV – additional volume of fluid introduced (ΔV1) into the subarachnoid cavity or "excess" volume (ΔV2), which is extracted from the subarachnoid cavity, causes ΔP
qp – changes in the rigidity of the craniospinal cavity

Ra – sensor indicator, installed on the cerebral cranium for detecting
RW – relative weight
SS – superior sagittal sinusSSP – sagittal sinus pressure
SW – specific weight
VP – systemic venous pressure

On the pathogenesis of various forms of an acute increase in intracranial pressure (ICP)

The sharp rise of ICP is a cause of unfavorable course of the acute closed brain trauma, acute brain herniation, intracerebral hematoma of different origin, and acute reversible vascular processes (certain forms of the hypertensive crisis, migraine-like syndrome).

The pathogenesis of acute increase of ICP has been discussed based on the analysis of clinical observations of the acute closed brain trauma [1-3], acute cerebral hypertensive crisis [4], and based on the experience of our scholars on inducing an acute brain herniation [5-8].

Acute brain trauma (ABT)

A pattern of the changes in mechanical conditions of the craniospinal system (CSS) during the ABT was investigated by using the previously described methodologies [1, 9-11].

A change in the cerebrospinal fluid (CSF) pressure is persistent during the ABT, as shown in Table 1. The prevailing kind of pathology is hypertension, which reaches 800-900 mm H2O in severe injuries. Hypertension is observed in all cases in acute brain compression, most of which are in an intense form. This is due to joining the primary pathological process caused by brain trauma and brain hemorrhage. The brain hemorrhage makes changes in CSF pressure more complicated. Polarization of alterations in CSF pressure occurs with severe brain trauma – the frequency and severity of CSF hypotension increase along with a higher rate and severity of CSF hypertension. A counterintuitive phenomenon occurs: a negative pressure that reaches minus (negative) 150 mm H2O has arisen. One is under the impression that polarization is a consequence of the phase transition of hypertension to hypotension since the increased frequency of hypotension occurs with the decreased frequency of CSF pressure, such as in the group with a severe brain contusion.

Table 1

CHANGES IN THE CSF PRESSURE IN ACUTE CLOSED BRAIN TRAUMA, FREQUENCY IS GIVEN IN % (RANGE OF M±1,5 G IN A CONTROL GROUP (HEALTHY PEOPLE) IS A REFERENCE CATEGORY)

The severity and nature of an injury		No. of investigated	Change pattern of ICP (CSF pressure)					
			Normal (%)	Hypertension			Hypotension	
				Total (%)	including		Total (%)	minimum pressure (mm H2O)
					within (mm H2O)	%		
Control group		81	88,9	9,8	-	-	1,3	160,0
Brain concussion		142	32,6	61,3	370-400	2,8	6,1	54,0
Brain contusion	mild	49	21,3	72,6	370-550	46,9	5,9	150,0
	moderate	50	21,5	72,6	370-650	39,2	5,9	-70,0*
	severe	48	8,3	64,6	370-900	45,8	27,1	-150,0*
Acute brain compression (hematoma)		46	-	100,0	370-800	93,4	-	300,0

**-negative pressure level.*

We consider that the phase transition is a critical element in understanding the pathogenesis of an increase of intracranial pressure in ABT. Decrease of CSF pressure, therefore, without any doubt, caused by the reduction of the craniospinal cavity content. This excludes the probability of brain volume reduction and its blood filling. The probable cause is a reduction of the cerebrospinal fluid volume. Meanwhile, there is no reason to consider that reduction in CSF volume is a consequence of the CSF resorption increase. Conversely, low-pressure resorption must be decreased. Consequently, a decrease in CSF volume in ABT that leads to a reduction of ICP can be explained by the depression of the glandular system of the choroid plexuses, which produce CSF. If the CSF hypotension caused by depression of the choroid plexuses is the final phase of the pathological process, then following the parabiosis and paranecrosis dynamics, which precede the hypotension of pathology, the function of producing CSF is supposed to be initiated, which in turn leads to CSF hypertension. It should also be noted that a malfunction of producing CSF in ABT is in all likelihood related to the nerve centers' damage where the phase of the pathological process occurs, which is ultimately cause the changes of intracranial pressure.

Therefore, various modifications of ICP (i.e. CSF pressure) occur depending on the severity of the injury of nerve centers in ABT: for mild and moderate injuries – different levels of CSF hypertension, and for severe injuries of the nervous system such as extremely high ICP and a polar form of changes – intracranial hypotension.

Brain swelling and an increase in its blood volume, as well as the changes in cerebrospinal fluid volume, can result in the changes of ICP during the ABT.

Physicochemical characteristics of the brain can be described through the changes in the rigidity of the craniospinal system (CSS) (Table 2).

Table 2

CHANGES IN THE RIGIDITY OF THE CRANIOSPINAL CAVITY – QP (AN INDICATOR OF THE CSF PRESSURE IS LEVELED) IN ACUTE CLOSED BRAIN TRAUMA, FREQUENCY IS GIVEN IN % (RIGIDITY COEFFICIENT QP OF 0,146±0,03 IN A CONTROL GROUP IS A REFERENCE CATEGORY)

The severity and nature of an injury		No. of investigated	Change pattern of the rigidity of CSS			
			Normal	Increase	Decrease	Total
Control group		81	86,4	12,3	1,2	100,0
Brain concussion		142	17,6	65,3	7,7	100,0
Brain contusion	mild	49	20,4	65,3	14,3	100,0
	moderate	51	17,7	72,5	9,8	100,0
	severe	48	16,6	61,3	22,9	100,0
Acute brain compression (hematoma)		46	6,5	87,0	6,5	100,0

In particular, the increase of the rigidity in ABT should reveal the brain swelling. There were frequent changes (of 79,6 to 93,5 cases) of the rigidity of CSS in all ABT forms. The prevailing form of change was an increase in the rigidity of the content of the craniospinal cavity (CSC). As the injury severity increases, so does a frequency of the rigidity of the content of CSC (q), as well as the level of severity of increase in rigidity. Thus, the coefficient of rigidity may show a 2- to 3-fold increase compared to standard indicators in severe ABT. This occurs because the ICP (PB) increases progressively with the growth of the severity of injuries. A residual pressure (PR) decreases at the same rate, the indicator of which approaches zero occasionally. As a result, the meaning of PB:PR rises dramatically.

As in changes in CSF pressure, the polarization of the changes in rigidity of the CSC was also observed during the ABT. Cases of rigidity decrease in CSS rises as the severity of injury increases. In severe

brain contusion compared to the less severe ABT, the increased frequency of rigidity decrease in CSS is taking place in conditions of reducing in the frequency of rigidity increase, which may be explained by phase pattern of changes of elastic deformation of the CSC content.

A phase of decreases of rigidity in CSS in a severe patient with a severe brain injury is explained by the non-reactive condition of a human organism, and it thus is a sign of lack of standard, i.e., physiological response to trauma leading to a brain swelling. Furthermore, the mechanism of rigidity decrease in CSS appears to be relevant to the non-reactive vascular system, which appears with a vasorelaxation with venous congestion. The data on a combination of changes in CSF pressure and rigidity of CSS are given in Table 3. It shows that abnormalities of the mechanical properties of CCS occur in a 100 percent of the cases of moderate and severe brain contusions and acute brain compression, in 93,9 percent of a mild brain contusions cases, and 89,5 percent of cases of brain concussion. Changes in the rigidity of CSS appear earlier than changes in CSF pressure. This is confirmed by the following: rigidity of CSS increases in 57,1 percent of cases of brain concussion while the CSF pressure decreases or has no changes. The most pathognomic is a simultaneous increase of CSF pressure, and rigidity coefficient of CSS, the frequency of which rises depending on the severity of an injury.

Table 3

THE CHARACTER OF A COMBINATION OF CHANGES IN ICP-PB AND RIGIDITY OF CSC CONTENT - QP (THE IMPACT OF ICP ON RIGIDITY (Q) IS LEVELED) IN ACUTE CLOSED BRAIN TRAUMA, FREQUENCY IS GIVEN IN % (N IS NORMAL; PB OR QP>N IS ABOVE NORMAL; PB OR QP<N IS BELOW NORMAL)

The severity and nature of an injury		PB>N and qP>N	PB=N and qP>N	PB>N and qP=N	PB<N and qP<N	PB=N and qP=N	PB=N and qP<N	Total
Brain concussion		17,6	57,1	9,3	1,4	10,5	4,2	100,0
Brain contusion	mild	38,8	26,5	22,5	-	6,1	6,1	100,0
	moderate	52,9	19,6	19,7	5,9	-	1,9	100,0
	severe	48,8	12,4	18,0	20,8	-	-	100,0
Acute brain compression (hematoma)		87,0	-	13,0	-	-	-	100,0

The high ICP, being a symptom of a disease, may also cause the nervous system irritation and alteration. The severe elevated ICP is considered to be the cause of death in traumatic, epi- and subdural hematomas [12-14]. An increase in ICP contributes to compression of brain vessels. It has been reported that high CSF pressure declines a venous blood outflow and complicates an arterial blood supply of nervous centers [14, 15]. Hypoxia due to compression of the brain vessels by edema causes tissular necrosis in acute brain trauma [12]. A classical form of the influence of increased ICP on brain nervous centers is the so-called Cushing's phenomenon [14].

In summary, it should be noted that an ongoing phase-pathological process in the nerve centers underlies the changes in the physicomechanical properties of CSC content in acute closed brain trauma. The first phase is manifested by the increased CSF production and brain swelling, so that increase in ICP and the rigidity of CSS occurs. It is more often an initial reaction to the rise in ICP. A very severe ABT is characterized by a non-reactive condition of an organism, in which an organism has no normal physiological response to the mechanical brain alteration. Intracranial hypotension and a decrease in the coefficient level of the rigidity of CSS replace intracranial hypertension and an increase in the rigidity of CSS during the mechanical brain alteration. In reality, however, the transition from one form of pathological process to another might does not occur outwardly. The change might be fleeting in severe injuries, and in very severe injuries, it might

start with a second phase with a poor prognosis. The reason for CSF hypotension in ABT is a combination of the cerebrospinal fluid and the lack of reactive brain swelling, which was caused by trauma due to paralysis of the brain centers. Decrease of the rigidity in CSS might be explained by decreasing of vessel tone or atony, venous congestion, and absence of edema in the brain matter.

Acute Brain Herniation

The enlargement of the brain with its prolapse into the trephine hole of the skull could be a complication during neurosurgical procedures in basal area of the brain. An extremely high intracranial pressure with a risk of suppression of the activities of vital centers is a grave complication of brain injuries affecting a basal area of the brain. This phenomenon was called "Acute brain swelling" initially [16]; however, later studies used the term of "Acute Brain Herniation" (ABH) [17-19]. Most investigators have concluded that the pathogenesis of ABH is based on neuroreflectory vascular response [6, 8, 17, 20-22]. The pathogenesis of brain herniation has also been explained by its acute swelling [16, 19, 23]. According to the results of our recent study, an increase in CSF production is involved in the pathogenesis of brain herniation substantively [6, 24].

There are three formable volumes in the craniospinal cavity with a rigid bundle bone: a brain tissue with shell, bloodstream, and cerebrospinal fluid. Under normal conditions, these volumes are balanced; once one of them increases, the others change.

Changes in all these three volumes probably contribute to an increase in the volume of CSC content in acute brain herniation. The question then becomes, what is the primary, and what is the secondary? Meanwhile, the current scientific conflicting viewpoints are mutually exclusive and preclude the study of the pathogenesis of brain herniation. Therefore, the problem remains unresolved.

We studied the pathogenesis of the acute brain herniation for several years. The results are summarized in this paper.

Research Methodology

According to the method described in the literature [25], acute brain herniation (ABH) was induced by stimulation of the hypothalamic region in adult dogs by injection of 40% formalin solution (0.1-0.2 ml). The injection was via a burr hole, which was immediately closing tightly. Several observations revealed that after the formalin injection, some dogs had developed impairment of respiratory function. In such cases, the dogs were transferred to mechanical ventilation.

Different parameters of vital signs were recorded: in an initial state and on2 (two) and 6 (six) minutes after the formalin injection. For anatomical examination of the brain, dogs were investigated in 10 (ten) minutes after stimulation of the nerve center, and several indicators of the craniospinal cavity content have been studied in the late brain alteration. There was a control healthy adult dog group, and the trial was conducted under hexenalum anesthesia (30 mg/kg).

Multichannel Polyphysiograph was used to record the physiologic metrics. The pressure was measured using the pressure gauge with a high linear response and a constant chamber (0.001 ml/ 100 mmH2O).

A 'T' shape catheter was inserted into the carotid artery and jugular vein to measure the systemic arterial (AP) and systemic venous (VP) blood pressures. Intracranial venous pressure (IVP) in the dural sinuses was measured with the puncture of the sinus using a specific puncture needle via the cranial trepanation of the superior sagittal sinus (SS). Defects on the skull bone were covered with plastic corks. Intracranial pressure (ICP) has been observed via cisterna magna puncture (21 gauge needle). Intraocular pressure (IOP) observed via anterior chamber. Sensors for measuring AP, VP, SSP, ICP, and IOP were fixed at the spinous process of a vertebra in a side-lying position. The specialized sensor in a chest measured a respiration rate. The body temperature was controlled and maintained at 37.5±0.5ºC by an electro thermometer.

Various methods have conducted a study on the blood supply of the brain:

1. The labeled (Cr-51) erythrocytes were injected into the bloodstream, and the amount of blood (ml) per 100 g of the brain tissue is subsequently determined (CrE).
2. The labeled (with iodine-131) seralbumin was injected into the blood:
   a) Detecting the radioactivity was carried out using a sensor in one trial, which installed on the cranial part of the skull (Ra);
   b) In another trial, the brain tissue penetrance coefficient (PC) was detected.
3. Rheoencephalography – IR – Integral rheogram.

The fluid in the brain matter was investigated by identifying the dry residue of the brain (DR, %). The sample was cooled in a desiccator to a constant weight at a temperature of 90-100 degrees centigrade and a relative weight in a mixture of bromobenzene and kerosene with a proportion of 1,024 to 1,044 (RW).

The rate of CSF production and CSF resorption was assessed by methods that have been developed at our laboratory.

Changes in AP, VP, SSP, ICP, and IOP, and rigidity of CSC content (q) in acute brain herniation

As Table 4 shows, an increase in intracranial pressure (ICP) is not the only sign of acute brain herniation (ABH). Additionally, an increase in SSP, IOP, VP, AP, and FP arises. Accordingly, ABH is a combined pathology of acute circulatory failure and CSF-dynamic disturbances. An increase in ICP, however, remains the main sign of ABH. The mean value (M) of ICP in ABH increases by 5 to 20, 3 times. An increase in ICP is followed by increases in SSP, FP, VP, IOP, and AP according to its value (from most to least). These indicators, except AP, were towards increasing. AP was polar in some instances. Thus, according to one of the 6-part series trials (part I), AP had increased reaching the average of 148±16,5 mm Hg in about half of cases, and in the other half, it had decreased earning the average of -99±6,4 5 mm Hg.

The duration of the latent for changes of indicators in ABH was studied in the first part of the trials (Figure 1). Figure 1 shows that the changes in intracranial pressure (ICP) and in venous pressure in the sagittal sinus (SSP) occur alongside with stimulation, rheo-encephalogram has also been changing at the same time (is not illustrated in Figure 1). Some indicators have been revealed to have a latent period: for VP is 61,6±21,1 seconds, for IOP is 64,1±19,6 seconds, and for AP is 65,2±21,5 seconds (are highlighted in bold in Figure 1).

Indicators reached a maximum value after a certain time of the stimulation of nervous centers in the following sequence: ICP – 230,9±31,8 seconds; IOP – 237,7±49,2 seconds; SSP – 244,3±24,6 seconds; AP – 246,3±32 seconds; and VP – 255,3±59,8 seconds.

Table 4

CHANGES IN BLOOD PRESSURE AND CEREBROSPINAL FLUID IN ACUTE BRAIN HERNIATION (M±M)

Trial series, number of experimental subjects, and (investigators)	Indicators and conditions of obtaining the data	mm H2O				mm Hg	
		ICP	SSP	IOP	FD	VP	AP
						System blood pressure	
1	2	3	4	5	6	7	8
I; n=13; (T.A. Makham-betov and E.S.Nur-guzhayev)	Baseline data, M±m	119,0±9,9	85,0±5,6	191,7±22,4	34,0	56,3	108,6
	In 4-6 minutes after alteration, M±m	578,2±57,7	422,9±73,3	453,1±4,2	155,3	200,0	96,0
II; n=9; (S.A. Zhanaidarov, S.M. Mausin-bayeva, and U.S. Sydykov)	Control data, M±m	71,8±6,0	-	-	-	-	100-110
	In 6 minutes after alteration, M±m	472,0±134,4	-	-	-	-	-
	Maximum value	1340,0	-	-	-	-	200
III; n=20; (S.A. Zhanaidarov, S.M. Mausin-bayeva, and U.S. Sydykov)	Control data, M±m	109,2±18,7	-	-	-	-	-
	In 10 minutes after alteration, M±m	321,8±49,8	-	-	-	-	-
	Maximum value	760,0	-	-	-	-	-

IV; n=9; (S.A. Zhanaidarov)	Baseline data, M±m	115,2±12,2	-	-	-	-	110,6±7,3
	In 5 minutes after alteration, M±m	828,9±196,6	-	-	-	-	133,0±28,4
	Maximum value	2350,0	-	-	-	-	220,0
1	2	3	4	5	6	7	8
V; n=9; (B.A. Atchabarov, B.A. Abeyov; and U.S. Sadykov)	Baseline data, M±m	129,4±13,8	111,3±12,8	-	18,1±2,2	53,8±7,2	114,4±2,0
	In 6 minutes after alteration, M±m	670,0±73,2	416,0±46,0	-	254±75,4	140,5±23	171,9±6,7
	Maximum value	1010	600	-	603	250,0	200,0
VI; n=11; (B.A. Atchabarov, B.A. Abeyov; and U.S. Sadykov)	Baseline data, M±m	127,5±7,8	106,7±10,8	-	20,4±3,1	34,0±5,3	116,4±7,6
	In 6 minutes after alteration, M±m	369,6±36,3	205,8±21,6	-	163,8±24,7	113,3±7,8	155,9±6,8
	Maximum value	615	358	-	295,0	140	200
Total	No. of times when "M" (average value) of the intervention group outnumbered the control (or group at baseline)	2,5-2,7	1,9-5,0	2,4	4,5-14,7	2,6-3,5	0,8-15
	No. of times when a maximum value of intervention group outnumbered the control (or group at baseline)	5,0-20,3	3,3-5,4	-	14,5-33,3	4,1-4,6	1,7-2,0

Thus, although in ABH, along with changes in intracranial hemo- and cerebrospinal fluid dynamics, changes and indicators of systemic circulation are also observed, the analyzed data indicate that changes in ICP, SSP, and FD is a leading increase, i.e. act as supreme: it arises immediately after the stimulation with no latent period and reaches the life-threatening critical value quickly. The ICP thus increases and reaches an 828,9 mm H2O on average, and 2350 mmH2O in maximum. Meanwhile, according to our data, a damaging impact of a high CSF pressure on the vasomotor center (in a dog experiment) occurs when the pressure is below 700 mm H2O. A pressure above 900-1000 mm H2O causes death in animals.

Before the study of the pathogenesis of high ICP in ABH, we should discuss the pathogenesis of increased SSP in ABH, as the changes in these indicators are similar.

It has been established that both the ICP and the pressure of intracerebral arterial vessels have an integral effect on SSP [26, 27]. The reason is that dural brain sinuses are collectors, which receives CSF from the subarachnoid cavity and blood from brain veins. As a result, the higher the ICP and the pressure of intracerebral veins, the higher the SSP. Additionally, to an increase of ICP due to brain enlargement, the pressure from the brain is added along with a growth in fluid volumes in the sinuses. This leads to reducing or compression the sinuses cavity and the pressure increase in it, and the similarity between changes in ICP and SSP, therefore, becomes apparent.

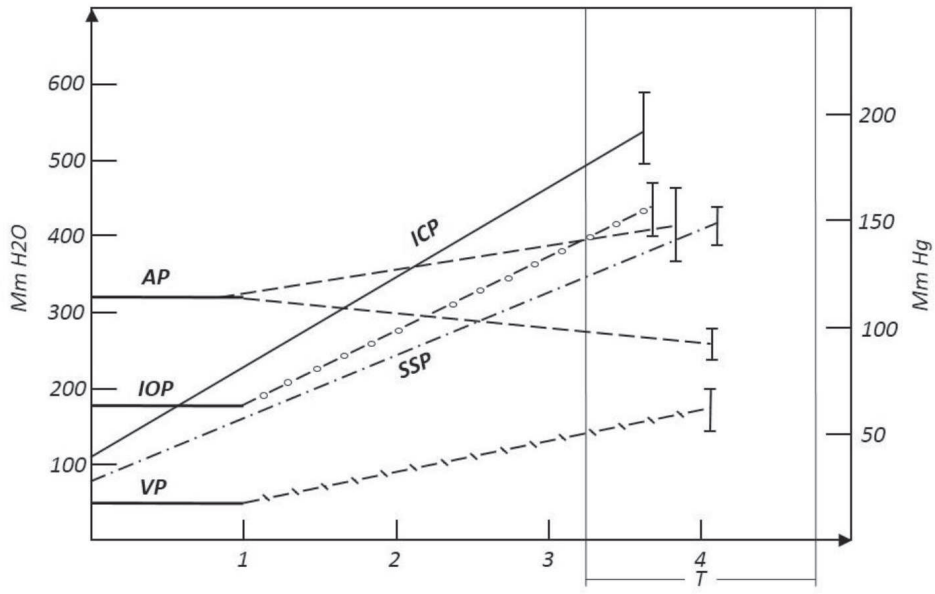

Figure 1 - The duration of the latent period (M±m) for changes and reaching the maximum values in ABH

Legends:
X coordinate is time in minutes;
Y coordinate shows a value of indicators;
"T" is a time when pressures reached the maximum;
AP – systemic arterial pressure;
SSP - venous pressure in the sagittal sinus;
VP – systemic venous pressure;
Bolded lines in AP, IOP, and VP –latent period;
Y coordinate: on the right – in mmHg for AP;
on the left – in mmH2O for ICP, IOP, SSP, and VP.

Table 5 shows that the indicator of rigidity, i.e., the coefficient (q) of the craniospinal cavity content in ABH, is 2-3 times greater compared to control group.

Table 5

CHANGES IN RIGIDITY COEFFICIENT (Q) OF THE CRANIOSPINAL SYSTEM AFTER AN ACUTE BRAIN HERNIATION (M+M)

After the start of ABH, in minutes	Groups	No. of exp.animals	q (mm/mm³)
60	Control	16	0,16±0,009
	Intervention	10	0,34±0,03
120	Control	16	0,21±0,01
	Intervention	10	0,47±0,05
180	Control	16	0,23±0,01
	Intervention	10	0,47±0,05
240	Control	16	0,25±0,02
	Intervention	20	0,8±0,07

It is difficult, however, to consider the true value of rigidity increase in CSC based on data given in Table 5. Because a given q coefficient in Table 5 is not a qP coefficient, in which the value of ICP is leveled. Some increases in q may be due to the high ICP, as the value of ICP is high in ABH. Therefore, given data

indicate only certain changes in the rigidity of the CSC content in ABH.

The same cause factors may influence the increase in rigidity of CSC and increase of ICP in ABH since both the ICP and the ABH are consequences of mechanical stress in CSC due to an increase in its content. It is unclear which increase in the craniospinal cavity causes this phenomenon, and which do not: either a brain enlargement due to brain swelling or an increase in circulating cerebrospinal fluid, or an increase in the blood supply of CSC content? Furthermore, the combination of these causative factors likely provokes the ABH collectively.

Brain swelling as a causal factor for the acute brain herniation (ABH)

The rational explanation for the ICP increase was the occurrence of acute brain swelling at the early stages of the study of the ABH. It has already been stated that some scientists take this view nowadays. If the brain swelling is involved in the pathogenesis of the ABH, then an increase in fluid content and a decrease in the specific weight of brain matter should occur.

Table 6 indicates the data of two series of trials on studying the fluid content of the brain matter during the ABH. Changes in the dry residue (DR) and a specific weight (SW) of the brain matter found to be unreliable and insignificant compared to control. Particularly, several series of trial reveal a slight decrease in brain tissue density, which points to a slight swelling process of the brain. Data on the rigidity of the CSC content show no severe swelling in the brain during the ABH. Therefore, the literature's explanation of ABH that defines it as the occurrence of rapid brain swelling seems hypothetical and unfounded factual material.

Table 6

CHANGES IN THE FLUID CONTENT OF THE BRAIN MATTER DURING THE ABH, (M+M)

Series of trial	Groups	Dry residue (DR), %			Specific weight (SW), g/cm³		
		Gray matter	White matter	The whole-brain	Gray matter	White matter	The whole-brain
II	Control (n=15)	18,0 ±0,18	32,11 ±0,40	20,81 ±0,28	1,041 ±0,0003	1,041 ±0,0002	1,039 ±0,0004
	Intervention (n=9)	18,25 ±0,22	31,55 ±0,38	22,36 ±0,25	1,042 ±0,0005	1,041 ±0,0004	1,040 ±0,0007
III	Control (n=10)	18,31 ±0,24	32,01 ±0,53	-	1,038 ±0,0006	1,039 ±0,0005	-
	Intervention (n=20)	17,42 ±0,20	30,06 ±0,38	-	1,036 ±0,0004	1,035 ±0,0006	-

Our results are in line with other scientists' findings [23]. According to the literature, the fluid content of brain tissues has not changed considerably during the ABH (similar to our results). However, at the same time, a fluid redistribution in the structural formation of brain tissue has been found. Fluid content has reduced by 7-8% in intercellular space, and it has increased by the same percentage in cells. This leads to the edema process in cells with vacuolization of cell organelles. Such fluid redistribution is common to dysfunctions of ion channel in the cell membrane, which occur in various damages, including any inflammatory, toxic process. Such a kind of edema, however, is limited to cause an acute brain herniation.

Thus, having an as small size of edema as in encephalitis, a brain swelling in such condition perhaps cannot cause an acute brain herniation.

On the increase in the blood supply of the brain during the acute brain herniation

Studies on the brain blood supply reveal that the volume of brain blood increases in all the five series of trials (Table 7). The blood volume has doubled within the method of using the labeled erythrocytes and according to the permeation coefficient on gray matter (an increase in white matter is insignificant), and the volume has also increased according to the rheography results by 1,5 times and the activity of

labeled albumin on the skull by 1,2-1,3 times (at the average).

An increase in brain blood supply by 1,5-2 times should lead to a reduction in dimension (capacity) of the craniospinal cavity (CSC) and an inevitable rise in ICP. Kovalev has reported [20] that an increase in the blood supply of CSC during the ABH arises due to hyperemia of the meninges, hyperemia the small-sized blood vessels of the brain, and diapedetic micro focal hemorrhage.

Table 7

CHANGES IN THE BLOOD SUPPLY OF THE BRAIN DURING THE ACUTE BRAIN HERNIATION, M±M

Set of trials	Groups	Indicators of brain blood supply				
		Blood supply, ml/100g of brain tissue (method of the labeled erythrocytes, Cr-51)	Integral rheogram (IR), (Δ r/r, %)	Re-activity of the labeled albumin J-131 on the skull, impulse / second	Penetrance coefficient (injection of the labeled (with iodine-131) seral-bumin)	
					Gray matter	White matter
II	Control, n=14	0,95±0,1	-	-	-	-
	Intervention, n=9	2,03±0,23	-	-	-	-
III	Control, n=9	-	-	-	0,97±0,16	1,06±0,2
	Intervention, n=15	-	-	-	2,09±0,25	1,27±0,13
	Baseline, n=9	-	0,429±0,041	-	-	-
IV	Five minutes after alteration,	-	0,648±0,130	-	-	-
	Baseline, n=8	-	-	349,8±47,9	-	-
V	Six minutes after alteration,	-	-	443,5±55,5	-	-
	Maximum value	-	-	746	-	-
	Baseline, n=11	-	-	293±37,0	-	-
VI	Six minutes after alteration,	-	-	344,8±43,0	-	-
	Maximum value	-	-	509	-	-

On changes in cerebrospinal fluid production and resorption during the acute brain herniation

Data on changes in CSF production during the ABH are given in Table 8. According to those data, a volumetric rate of CSF production has increased by 1,7 times versus the normal indicator in two minutes after brain alteration, by 4,6 times after six minutes. It has increased eightfold and reached a maximum in trial N 5, and trial N 10 shows a ten times increase.

Table 8

THE INFLUENCE OF ALTERATION ON A VOLUMETRIC RATE OF CSF PRODUCTION AND ARTERIAL PRESSURE (AP)

Serial number of an animal		CSF production rate, in ml · min^{-1}			AP, in mmHg		
		Baseline	Time after alteration, in minutes		Baseline	Time after alteration, in minutes	
			2	6		2	6
1		0,06	0,11	0,18	120	135	150
2		0,11	0,09	0,36	105	190	160
3		0,09	0,11	0,24	110	90	130
4		0,24	0,24	0,48	110	220	170
5		0,11	0,72	0,90	130	100	160
6		0,09	0,03	0,42	130	100	200
7		0,11	0,06	0,42	120	150	150
8		0,06	0,24	0,42	115	140	140
9		0,18	0,3	0,54	115	130	145
10		0,06	0,42	0,6	120	180	180
11		0,11	0,18	0,48	105	120	130
Total	M	0,11	0,21	0,51	116,4	141,5	155,9
	±m	0,017	0,062	0,062	7,62	12,4	6,4

It should be noted, an increase in CSF production occurred in six minutes after alteration in all experimental animals, but in two minutes, only in half of the animals.

When assessing the changes of CSF resorption by the filtering pressure (FP), a CSF outflow first increases, but do not decrease, despite the increase of pressure in the superior sagittal sinus. A volumetric rate of CSF production in our experimental animals, therefore, should be slightly higher than those indicated in Table 8.

Our study suggests that, on the one hand, a high ICP during ABH is caused by an increase in the volume of CSF due to increasing the speed of its production, and, on the other hand, by an increase of the blood volume in the brain. However, it is difficult to provide accurate indications about the impact of an increase in CSF production and blood volume on ICP. Our study, therefore, aimed to find the proportion between the increase in CSF production and blood volume in craniospinal cavity. A set of trials (V and VI) was carried out to answer the research question.

The outflow (drainage) of cerebrospinal fluid with a determination of its volumetric rate from the lateral ventricle was conducted on test animals with ABH in VI trial. The trial V with no drainage was a control group for trial VI. A comparison of the data on these two series trial is given in Figure 2.

Figure 2 shows that the increases in ICP in trial V were 2,2 times higher than in trial VI. Similarly, SSP was 2,2 times lower in trial VI compared to trial V. There was no significant difference between the remaining indicators (AP, VP, and Ra).

It would thus appear that an increase in CSF volume is more impactful than an increase in the blood volume in the CSC and the value of brain swelling combined although the rise in blood volume itself in CSC may be significant in increasing the production of CSF.

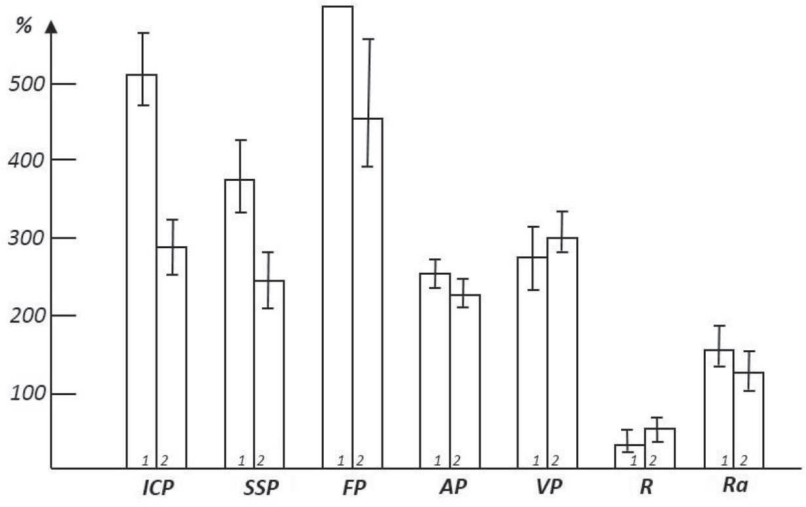

Figure 2 – Difference between hemodynamic and CSF circulation in trial series V and VI on test animals in six minutes after hypothalamus alteration

Legends:
X coordinate is the assessed indicators;
Y shows a degree of change, in %, 100 is a baseline;
ICP – intracranial pressure;
SSP – blood pressure in the sagittal sinus;
FP – filtrating pressure;
AP – systemic arterial pressure;
VP – systemic venous pressure;
R – respiratory rate;
Ra – radioactivity on the skull;
1 – V series of trials;
2 – VI series of trials.

Furthermore, the data of the V and VI series of the trial indicate that the CSF drainage during the acute brain herniation has a positive therapeutic effect (reduced ICP and improved breathing).

The correlation between the hemodynamic and CSF circulation was calculated for clarifying the reasons for changes (based on the data obtained in the V and VI series of trials) (Table 9).

A positive average and above-average correlation was found between ICP, SSP, and Ra. This association suggests a blood supply of the brain (Ra) to be a probable causative agent for changes in ICP and SSP and the causation of SSP from ICP.

Table 9

CORRELATION COEFFICIENTS

	Correlation between:	**V trial (n=8)**	**VI trial (n=11)**
1.	ICP and Ra	+ 0,54	+ 0,57
2.	ICP and SSP	+ 0,53	+ 0,46
3.	ICP and AP	+ 0,08	+ 0,03
4.	ICP and VP	+ 0,2	+ 0,5
5.	SSP and Ra	+ 0,63	+ 0,63
6.	SSP and VP	+ 0,2	+ 0,5

7.	SSP and AP	+ 0,7	-0,1
8.	AP and Ra	-0,1	+ 0,4
9.	AP and CSF production rate	-	+ 0,07

The correlation coefficient between the intracranial hemo- and CSF dynamic indicators and the systemic arterial pressure (AP) demonstrates no correlation between the AP and ICP, between the AP and CSF production rate; and reflects the doubtful and controversial correlation between the AP and SSP, and between the AP and Ra.

Furthermore, data given in Figure 3 show no positive correlation and even a negative correlation between the AP and blood supply of CSC during the ABH. The changes in ICP and comparison of AP and IRH (rheoencephalogram) are given in Figure 3 (based on results of IV series of trials).

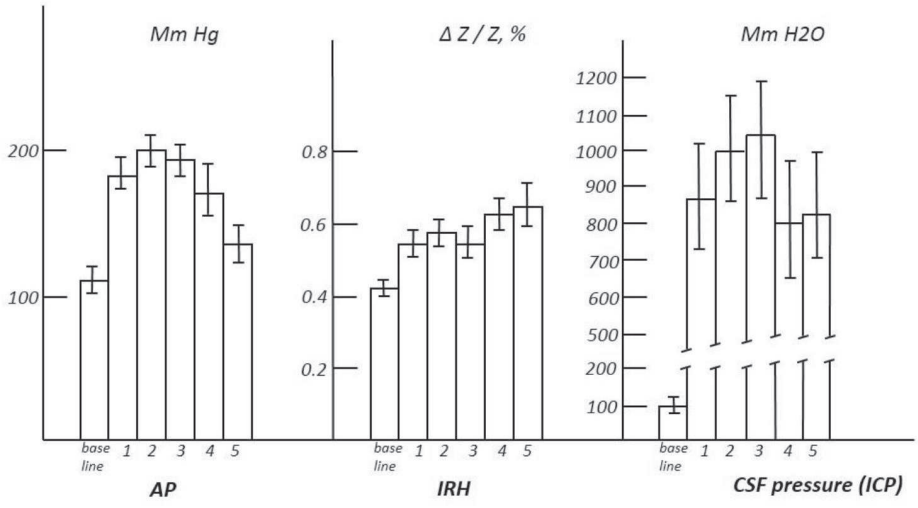

Figure 3 – Changes in certain physiological indicators during the acute brain herniation on experimental dogs of IV series of trials

Legends:

AP – arterial pressure (arteria carotis);

IRH – integral rheogram of the head (amplitude);

ICP – intracranial pressure;

X coordinate is the time (1- 5 minutes after stimulation);

Y coordinate is the value of indicators.

Thus, the correlation coefficient indicates that the changes in AP are insignificant or even negative within the hemo- and CSF dynamic shifts during the ABH. This correlations reveals a polar orientation of changes in AP and intracranial hemodynamic. This is explained by the following: the increase in systemic arterial pressure is the opposite process to the rise in CSC blood volume. While an increase in AP is caused by vasoconstriction, the vasodilatation gives rise to the blood volume of CSC. If these polar mechanisms come to the fore, the correlation will probably be negative. In certain cases, however, the correlation between AP, hemo and CSF dynamic might be weakly positive in case of ABH. This occurs because an increase in AP may also cause the intracranial hemodynamic disturbances since a high pressure contributes to the redistribution of blood from the zone of anemia to the hyperemia.

Pathogenesis of the ABH. Opinion on the nervous center that controls intracranial pressure and blood supply of the brain

The systemic arterial pressure is not the prime reason for the acute brain herniation and its signs (an increase in ICP, SSP, and blood supply of the CSC). An increase in systemic arterial and venous pressures and disturbance of intracranial hemo- and CSF dynamic during the ABH seem to be a related process, but they do not have any direct causal link. We consider that a vasomotor center that controls the AP is affected slightly during the acute brain herniation. However, all the pathological changes affect mostly the nervous centers, which regulate the intracranial hemo- and CSF dynamic.

The analyses reveal that an increase in ICP, which is a core sign of the ABH, is caused by the rise in the volume of CSF in the CSC due to its rapid production; increased blood volume of the brain; and in part, by an increase of the brain volume due to its slight swelling. Our impression was that an increase in CSF volume has greater importance than an increase in the blood volume of CSC and brain swelling combined (a blood supply of the CSC increases by 1,5-2 times, and a cerebrospinal fluid volume increases by 4,6 time in average, in some animals by ten times) during an increasing of ICP in the ABH. Based on the experiments, we conclude that a cerebrospinal fluid leak during the ABH can be a pathogenetic therapeutic activity (at least the growth in CSF pressure decreases by more than two times).

The general picture of the changes in hemodynamic during the ABH is first described as defense autoregulation disruption of the cerebral blood flow, which leads to the mismatch of local changes with changes in systematic circulation.

The system, which has an independent auto regulation mechanism, affects both a blood supply of the CSC (i.e., blood circulation) and CSF production. The mechanism limiting hemodynamic and CSF dynamics are within the narrow framework necessary for the normal functioning of the brain. A weakening or loss of the "local" autoregulation with the following disorder of cerebral circulation and pressure in CSC occurs due to the disruption of this mechanism.

Our views on the independent nervous center that controls the ICP (and therefore CSF production) and the blood supply of the brain are based on the following arguments:

1. Zero correlation between the ICP, blood supply of the CSC and the CSF production in one hand, and the AP level in the ABH on the other;

2. A syndrome similar to the ABH does not occur during the chronic Hypertensive Disease with a high AP. Moreover, not all patients with hypertensive crises have a syndrome of the acute increase in ICP.

3. Not infrequently, a relatively low AP occurs during the experimentally induced syndrome of ABH with uncontrollably high ICP.

An increase in ICP during the ABH exceeds the safe level, which is 500-600 mm H2O in dogs. Continuous cerebrospinal fluid drainage, therefore, is recommended for therapeutic purposes. The pathophysiological process is parabiotic during brain traumas. It has been revealed that the fluid moves from the extracellular space into the cell interior. These data suggest the functional abnormalities in the ion channels of cell membranes, perhaps due to insufficient energy supply. Therefore, a sufficient amount of adenosine triphosphate (ATP) is indicated for patients with the ABH.

Thus, an increase in CSF production speed and an increase in the blood volume of the brain are found to be a significant factor in increasing the intracranial pressure. Minor edematous changes in the brain are additional signs of the hemodynamic and fluid dynamic disturbances. We consider that the syndrome of acute brain herniation is associated with a dysfunction in autonomous nerve centers that keep the intracranial pressure at a normal due to the regulation of blood flow intensity in CSC and cerebrospinal fluid production.

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БАССҮЙЕК ІШІНДЕГІ ҚЫСЫМНЫҢ КӨТЕРІЛУ МЕХАНИЗМІ ЖӘНЕ ОНЫҢ МИ ТІНІНЕ КЕРІ ӘСЕРІ

Берілген мақала бұрын жарияланған академик Бахия Атшабарұлы Атшабаровтың монография бөлімінің қайта басылымы болып табылады. Дәйексөз келтіру мақсатында жұмыстың түпнұсқасына сілтеме келесі көрсетілгендей жүзеге асырылады: Атшабаров Бахия «Бассүйек ішіндегі қысым және ликвородинамика физиологиясы мен патофизиологиясы очеркі», Ғылым баспасы, 1996 ж., 201-226 бб.

1996 жылы басылымға шыққан монография автор және оның әріптестерінің қалыпты жағдайда және ауытқу жағдайындағы бассүйек ішіндегі қысымды зерттеуге бағытталған бұрын жарияланған ғылыми жұмыстарының жиынтығы болып табылады. Жұмыс бассүйек ішіндегі гипертензия туындауына әсер ететін түрлі факторларды, атап айтсақ, ликвородинамикалық бұзылымды, ми ісінуін, краниоспиналды қуыстың қанмен толтыруындағы өзгерістерді және артериалды қан қысымы өзгерістерінің салдарын сипаттайды. Сонымен қатар, ғылыми жұмыста цереброспиналды сұйықтық динамикасының (сұйықтықтың өндірілуі, айналымы және резорбциясы) физиологиясы мен патофизиологиясы зерттелінеді. Монографияда бұрындары белгілі болған және көп жылдар бойы жүргізілген ғылыми жұмыстың нәтижелері пайымдалады.

Негізгі сөздер: бассүйек ішіндегі қысым, мидың жіті жарығы, ми жұлын сұйықтығының динамикасы.

Б.А. Атчабаров (1919-2010)

МЕХАНИЗМ ОСТРОГО ПОВЫШЕНИЯ ВНУТРИЧЕРЕПНОГО ДАВЛЕНИЯ И ПАГУБНОГО ЕГО ВЛИЯНИЕ НА ТКАНИ МОЗГА

Данная статья является репринтом (переизданием, перепечаткой) ранее опубликованной главы монографии академика Атчабарова Бахии Атчабаровича «Очерки физиологии и патофизиологии ликвородинамики и внутричерепного давления», изд. Ғылым, 1996 г., стр. 201-226.

Изданная в 1996 году монография является обобщением ранее опубликованных исследований автора и его коллег, посвященных изучению внутричерепного давления в норме и при патологии. Описывается участие различных причинных факторов в возникновении внутричерепной гипертензии: ликвородинамические нарушения, отек-набухание мозга, изменения кровонаполнения в краниоспинальной полости и последствия изменений артериального давления. Исследованы также вопросы физиологии и патофизиологии продукции, циркуляции и резорбции ликвора. В монографии подвергнуты анализу и осмыслению ранее известные и полученные в ходе многолетних исследований собственные научные данные.

Ключевые слова: внутричерепное давление, острое пролабирование головного мозга, ликвородинамика.