HYDRAULIC "CEREBROPHTHALMIC LOOP" DETERMINING IN THE RELATIVE INTRAOCULAR HYPERTENSION MULTIPLE "NERVOVASCULAR CONFLICTS" IN THE SKULL, INCLUDING CAVERNOUS SINUS, ORBIT AND EYEBALL, COMPLICATING IN THE "VICIOUS CIRCLE" MECHANISM, DEPENDENT ON THE BERNOULLI'S PARADOX, ORGANISM'S LOCAL AND SYSTEMIC DISORDERS IN THE "4 LEAD 4 BRAIN" PROCESS BY NOGAL

I wish to give in your hands the promised publication about "The mechanism of periodic strabismus dependent on neurovascular conflicts in the cavernous sinus and superior orbital fissure, which are secondary to the intraocular hypertension in the posterior chamber and vitreous humour chamber of the eye by Piotr Nogal", which is actually identical, in terms of the causing agent and principles of action, to the described by me mechanisms of the Tolosa-Hunt syndrome, "idiopathic" cavernous sinus syndrome, "idiopathic" orbital apex syndrome, "idiopathic" superior orbital fissure syndrome, ophthalmoplegic migraine and trigeminal neuralgia, "idiopathic" - "malicious" exophthalmos and many other "idiopathic" so far disorders of the eye, orbit and brain (remaining as my discoveries in the area of the mechanism of "MIGRAINE" described by me ⁵). Therefore, I am forced to make the reader of this publication, who is not always a Doctor, familiar with the anatomy and physiology of the vascular connection between the cavernous sinus of the brain and the eyeball. Doctors will also find it helpful in refreshing the anatomical knowledge in this field and referring to the issue more easily. The aim of this publication is to explain a relatively complex mechanism which leads to hypertension in the vessels connecting the brain and the eye and to their extention resulting in various neurovascular conflicts in anatomical isthmi of the skull, through which these vessels pass. This connection is a very complex hydraulic formation, in which (arterial and venous) structures enclosed in the cavernous sinus are responsible for blood exchange between the brain and the eye, from which aqueous humour (regulating intraocular pressure) with venous blood also outflows into this sinus. Venous blood is immiscible physiologically with arterial blood, but due to the occurrence of the artery with its flexible walls in a closed venous space limited with relatively rigid walls, the pressures of these two structures influence each other, acting in terms of the pressure system as a "functional loop" (hence the term "hydraulic" was proposed by me)^{7,8}. This sounds complicated indeed, so I

 $^{\,1}\,$ The term "cerebrophthalmic hydraulic loop" proposed by the author, Piotr Nogal.

This refers to the hypertension that results in the equalisation of pressures in the posterior chamber and vitreous humour chamber with the one in the choroid as proposed by the Author in the paper "Nogal's mechanism of migraine "MIGRAINE" and primary open-angle glaucoma of "normal" pressure in the light of the "mechanical" and the "vascular" theory of the optic nerve damage" (presented during the Polish Ophthalmologists Convention in Wrocław in 2016, publication no. 5 on the website (http://nogalmedicine.pl/wp-content/uploads/2014/10/Nogals-mechanism-of-migraine-EN.pdf)

³ Daniel Bernoulli (born on 8th February 1700 in Groningen, died on 17th March 1782 in Basel) - a Swiss mathematician and physicist. He was professor of mathematics in St Petersburg from 1725 and professor of anatomy and botany at the University of Basel from 1733. He did not accept the chair of the faculty of physics there until 1750. The creator of the foundations of statistical mechanics (the kinetic-molecular theory of gases). He was also interested in medicine and physiology. As a mathematician he dealt with the probability theory, differential equations and approximate methods of solving equations. He defined the number "e". As a physicist he solved the problem of vibrating strings and gave the equation for the stationary motion of an ideal fluid called Bernoulli's equation. He also considered the problem of the St. Petersburg paradox (first offered by his cousin Nicolaus Bernoulli I) and found its solution, with which he created the foundations of the expected utility theory (using this method three economists won the Nobel Prize awarded by the Bank of Sweden). He also discovered that fast moving fluid (liquid, gas or plasma) poses a lower pressure when moving slower (based on Wikipedia).

⁴ "4 lead 4 brain" ("quadruple load for the brain"; "4 x Pb for the brain"; (Pb - lead in the Mendeleyev periodic table). The term proposed by the Author for the raised pathophysiological mechanism. Described in the further part of the paper.

⁵ The mechanism of migraine dependent on the relative intraocular hypertension was presented by me during the symposiums "Ophthalmologic Surgery 2014 in Katowice" and in 2016 in Wrocław. It is also the subject of publication on this website, e.g. "Publication No. 5".

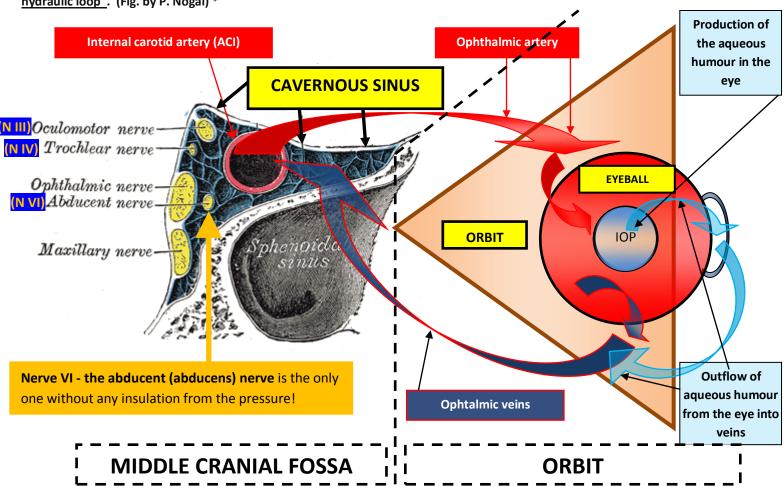
⁶ I explored the mysteries of human anatomy for one year in **AWF** [Academy of Physical Education] in Wrocław and for another year during medical studies at the **Faculty of Anatomy at the Military Medical Academy** in Żeligowskiego St. in Łódź, where being a student of this great university I had the honour to spend about a dozen hours per week during classes and lectures on the 1st year of studies at my medical Alma Mater. The faculty was run by the **Doctor of Medical Sciences Bohdan Zientarski** - a neurologist who put great emphasis in didactics on the difficult knowledge of CNS (central nervous system), including primarily the brain, which was our nightmare back then, but now makes me express my appreciation to Doctor, which I hereby do. Dr Zientarski is one of my masters of medicine and also the author of normal anatomy course materials: **"CNS - notes for students of the Faculty of Medicine at the Military Medical Academy"**.

⁷ The structure of the outflow of venous blood with aqueous humour from the eyeball into the cavernous sinus, through the lumen of which the internal carotid artery passes and introduces blood into the eyeball, provides for a relatively functionally closed hydraulic system. That's because the same amount of blood and aqueous humour as it outflows from the system must also flow into it and must be produced in it in order to maintain the relative physiological stability. This, however, impairs the occurrence of other branches of the ophthalmic artery and a different number of "emergency" arterial and venous anastomoses supplying the system and receiving from it fluids that generate hydrostatic pressure prevailing there (see Fig. 1)

decided that before publishing the article on the mechanism of selected cases of periodic strabismus from the "neurovascular" conflict in the superior orbital fissure and the cavernous sinus proposed by me, I will make you familiar with the anatomy and pathophysiology of the issue, dependent on the described laws of physics for hydrostatic and dynamic pressure contained in Bernoulli's equation and the hydrodynamic paradox described by him.

In order to get a better understanding of the hydraulic interdependence in the circulation of blood with aqueous humour between the brain and the eye⁹, which accounts for risk in such dynamic (periodic) pathophysiological changes, it is necessary to be aware of the structure of the flow path of these fluids. It is presented in the diagram below.

Fig. 1 Blood circulation between: cavernous sinus in the brain \rightarrow orbit \rightarrow eyeball \rightarrow orbit \rightarrow cavernous sinus; "cerebrophthalmic hydraulic loop". (Fig. by P. Nogal) *



*In the above figure a drawing of cavernous sinus by Henry Vandyke Carter - Henry Gray (1918) "Anatomy of the Human Body" was used.

The diagram above shows a specific situation of the physiological predisposition in which the increase in hydrostatic pressure in any of the shown interconnected structures (arteries, veins and the eyeball filled with aqueous humour and vitreous body) may lead to the "vicious circle" mechanism that not only leads to a clinically dramatic situation in the eyeball and orbit, but also in the brain, which could even pose a threat to life caused by intracranial hypertension and brain oedema, including brainstem herniation. The clinical evidence for such a possibility is e.g. carotid-cavernous fistula, which is a life-threatening condition in neuro-ophthalmology causing a significant increase in pressure in the cerebral circulation and intraocular hypertension or Nogal's mechanism of migraine "MIGRAINE" described by me¹⁰. The indirect evidence from the analysis based on anatomy, physiology and physics are the arguments below. The resulting pathologies determined by the fluids

⁸ The situation of the interaction between pressures of the venous and arterial system in the "cerebrophthalmic hydraulic loop" is gets even more complicated when the ophthalmic artery or its anastomoses (middle meningeal artery and branches of maxillary artery) remain in contact with ophthalmic veins in the superior orbital fissure, occurring there not permanently but quite often (e.g. ophthalmic artery in approximately 20% of the population).

The aspect of cerebrospinal fluid circulation has been deliberately omitted in this paper so as not to make the image of the essence of the described mechanism blurred. A paper with the author's hypothesis on the regulation of the outflow of all fluids from the eye is being prepared for publication and constitutes an innovative article on the pathophysiology of glaucoma. It is a part of the paper "POLAND - (Pump of Outflow Launched Actively Nogal Description) and has a chance to revolutionize the approach to the problems of retinal cells apoptosis and loss of fibers in glaucoma.

^{.0} Publication No. 5 on the website: http://nogalmedicine.pl/wp-content/uploads/2014/10/Nogals-mechanism-of-migraine-EN.pdf

flow disorder in the "cerebrophthalmic hydraulic loop" are presented in the diagram in Fig. 5. It also presents an example of uniform pathologies within a particular structure which emerge regardless of the location of the initial increase in hydrostatic pressure in the "cerebrophthalmic hydraulic loop" described above (cavernous sinus \rightarrow internal carotid artery and ophthalmic artery \rightarrow eyeball \rightarrow ophthalmic veins \rightarrow cavernous sinus). The diagram also illustrates the flexibility of the beginning of the loop disorders with uniform complications, which is caused by the "vicious circle" mechanism within its area.

In order to understand why in the described mechanism such a significant role is played by the pupillary block with secondary intraocular hypertension in the posterior chamber and vitreous humour chamber, increasing hydrostatic pressure in the entire "cerebrophthalmic hydraulic loop", it is necessary to relate Bernoulli's paradox to the circulation of the fluid between the eye and the cavernous sinus. The pioneering reference of this phenomenon to eye vessels and the discovery of its importance in the pathophysiology of many disorders that have remained unexplained so far is my next achievement on the way of searching for the cause of disorders that have been regarded as "idiopathic" so far 11. Therefore, I present below Bernoulli's equation and its practical explanation of the pressures paradox in the flow of fluids.

Bernoulli's equation:

 $\rho v^2 / 2 + \rho gh + p = const$ where :

 ρ - fluid density g - gravitational acceleration

p - fluid pressure v - flow velocity h - height in the reference system

This equation implements the universal principle of conservation of energy and despite the fact that in its main assumption it concerned the perfectly incompressible, stationary and non-viscous fluid (it is difficult to say this about different consistencies, mixing in vessels of the discussed system, aqueous humour and blood with its variable physico-chemical parameters), it can also be referred to non-perfect fluids, such as blood and even compressible gases.

For us Doctors its interpretation is important, which explains Bernoulli's paradox and says that if there is an obstacle on the route of the fluid moving with a particular speed (e.g. a septum on the route of the flow or a narrowing in the vessel in which it is moving), this causes the greatest inhibition of the flow and drop in the fluid velocity in front of the obstacle and its slighter slowing down behind the obstacle, which in both cases causes an increase in hydrostatic pressure (greater "in front of the narrowing"). In the narrowed segment, however, there is an equalizing acceleration of the fluid flow, which leads to the drop in hydrostatic pressure at that point. That is because the smaller fluid flow velocity in a particular location, the greater static pressure it generates. Therefore, a wing of an airplane that is convex toward the top produces lift force lifting the airplane, or when we blow air between two sheets of paper, paradoxically they come together (faster flow of air between the sheets reduces the static pressure between them and higher pressure on both external sides of the sheets compresses them towards the centre). I related this phenomenon to arterial vessels in the eyeball, primarily to the choroid, which after being compressed by the hydrostatic pressure of the posterior chamber and the vitreous humour chamber inside the eyeball¹² (in ophthalmological practice called by us "intraocular" have such totally narrowed cross-sections for the blood flow that it causes the need to increase velocity within them and makes them even more vulnerable to intraocular pressure growing in the mechanism of vicious circle.

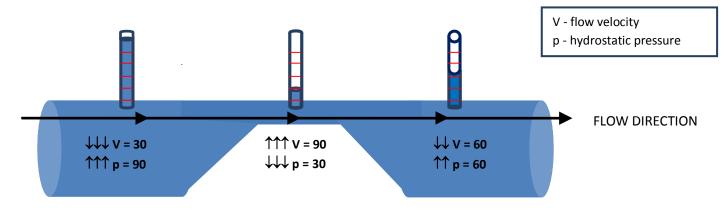
The diagram presented below:

¹¹ I do not believe in the existence of even a single "idiopathic" (without a reason) disorder, so I put this term between quotation marks.

The increased pressure in the eyeball must press the intraocular vessels located in the rear segment of the eye; they do not occur in the anterior chamber! There may be a situation when in post-trabecular open angle glaucoma without pupillary block there will be the simultaneous increase in both chambers of the eye: the anterior and the posterior ones, where pressure in the posterior chamber will equal (in total block of outflow from the eyeball) or higher in the posterior chamber, but when some amount of aqueous humour outflows from the eye conventionally.

¹³ Naming the static pressure in the eyeball "intraocular" is, in my opinion, an oversimplification of the issue of pressure in the eyeball, because inside the eyeball there are physiologically at least 5 pressure values in 5 separate hydraulic structures: 1) the anterior chamber, 2) the posterior chamber and the vitreous humour chamber, where pressures will be equal, 3) the central retinal artery, 4) the central retinal vein, 5) the choriocapillaris... The 6th structure will most likely be reviewed in one of the subsequent publications after having the issue discussed with my scientific Idol and highest Authority in the field of Glaucomatology.

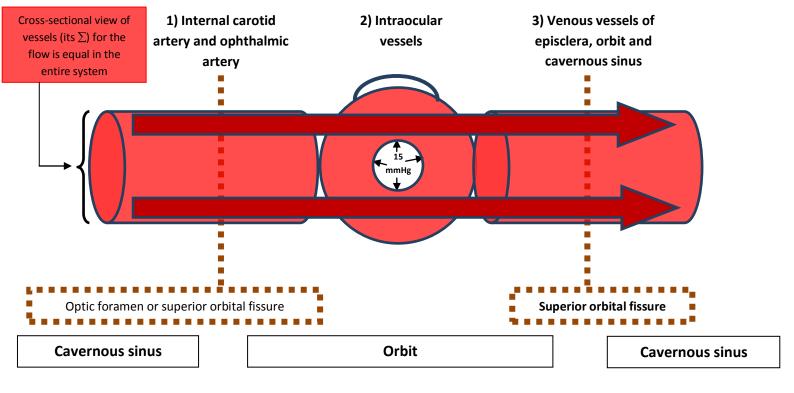
Fig. 3 Diagram showing Bernoulli's paradox in the flow of fluids. (Fig. by Piotr Nogal):



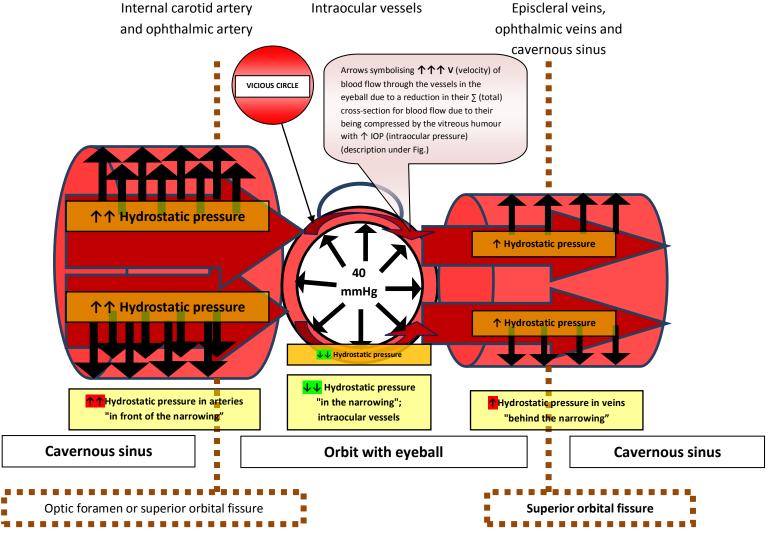
In order to understand why in the pathophysiological mechanism "4 lead (Pb) 4 head" described by me such a great role is played by the relative intraocular hypertension in the posterior chamber and vitreous humour chamber of the eye (e.g. in increased pupillary block), which raises hydrostatic pressure in the entire "cerebrophthalmic hydraulic loop", it is necessary to refer Bernoulli's phenomenon to the circulation of fluids between the cavernous sinus and the eye. The reference of this phenomenon to eye vessels and the discovery of its great importance in the pathophysiology of many disorders that have remained unexplained so far is my next achievement on the way of searching for the cause in disorders that have been regarded as "idiopathic" so far. I present these dependencies in the diagrams below.

Fig. 5: Bernoulli's phenomenon referred to the blood flow in the arterial and venous vessels of the eye inhibited by intraocular hypertension, compressing intraocular vessels (A - physiological condition, B - condition with intraocular hypertension in the posterior chamber and vitreous humour chamber of the eye with compression on vessels in the eyeball, shrinking their total cross-section for the flow). The reference of this phenomenon to the eye pathophysiology is a discovery made by Piotr Nogal. (Fig. by Piotr Nogal):

A - physiological condition; low IOP - intraocular pressure (15 mmHg) slightly compresses intraocular vessels (small black arrows in the lumen of the eyeball); does not interfere with the blood flow from the cavernous sinus into the orbit, through the eyeball back into the orbit and through the superior orbital fissure into the cavernous sinus; the blood flow through all the vessels is correct (red and blue arrows), on the red background symbolising a total of the cross-section of vessels in a particular segment)



- B pathological condition; intraocular hypertension (symbolic 40 mmHg in the middle of the eye) narrows the lumen of vessels in the eyeball, inhibiting the blood flow and acting as an "obstacle for the flow", causing the following pathophysiological changes in the flow:
- 1) greatest increase in blood pressure "in front of the obstacle for the flow" (in front of the eyeball): the ophthalmic artery and internal carotid artery become extended due to the pressure increase in their lumen,
- 2) paradoxical drop of the hydrostatic pressure "at the obstacle" (intraocular vessels; mainly the choroid) against the "quantitative equalisation" of the volume of blood flowing at the same time with increased flow speed through the "obstacle for the flow"; narrowed vessels in the eyeball,
- 3) increase in the pressure of blood flowing "behind the obstacle for the flow" (behind the eyeball in the orbit): the episcleral veins and superior and inferior ophthalmic veins become bloated due to the pressure increase in their lumen, determined under the pressure increase in ACI by an additional pressure spike in the cavernous sinus, into which they dissipate blood with aqueous humour from the eye and orbit.



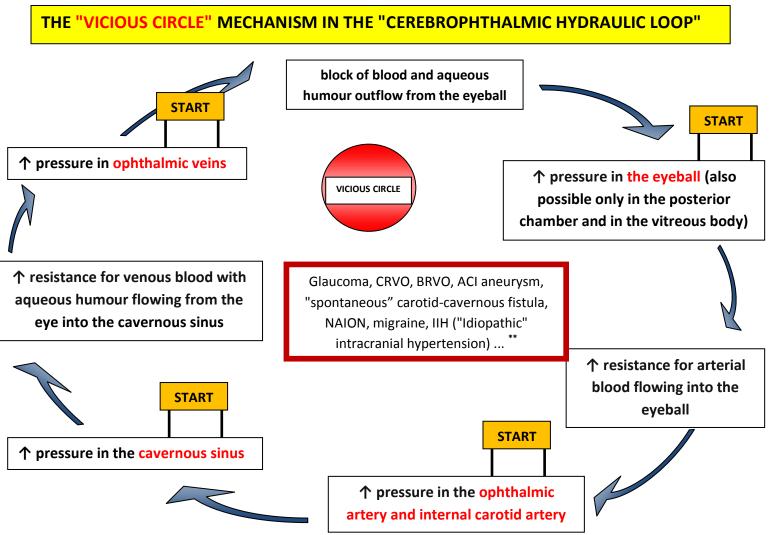
Description:

Red arrows (two) in each segment symbolise changes in $\uparrow V$ of the flow and hydrostatic pressure in a particular segment through the vessels in the eyeball due to a reduction of \sum (sum) of their cross-section for blood flow due to their being compressed by the vitreous humour with \uparrow IOP (the thicker the arrow, the greater hydrostatic pressure and slower flow). $\uparrow V$ of blood flow gives \downarrow hydrostatic pressure in intraocular vessels and begins another phenomenon of "vicious circle" (the more compressed intraocular vessels, the less flow lumen and lower pressure prevailing in them, which causes that even lower intraocular pressure can effectively clinically compress these vessels and lead to more intensive changes in the flow pressure and velocity determined by Bernoulli's paradox).

↑ IOP → ↓ total cross-section of vessels in the eyeball ("eye - dam" for the flow in the ophthalmic artery) → ↑ BP (hydrostatic blood pressure) in the ophthalmic artery and internal carotid artery → ↑ blood flow velocity and hydrostatic blood pressure drop in the vessels in the eyeball → ↑ hydrostatic blood pressure in the veins outside the eyeball → ↑ IOP →

The "vicious circle" mechanism already described above together with possible clinical situations, beginning according to Bernoulli's paradox in the "cerebrophthalmic hydraulic loop" described above (cavernous sinus \rightarrow internal carotid artery and ophthalmic artery \rightarrow eyeball \rightarrow ophthalmic veins \rightarrow cavernous sinus), is presented below on the diagram showing additionally the flexibility of the start of the loop disorders with as uniform as possible complications for a particular structure, distant from the beginning of the disorders.

Fig. 5 The diagram showing the "vicious circle" of pressure disorders in the "cerebrophthalmic hydraulic loop"; hydraulic structures of the loop marked in red, where the pathological mechanism begins. (Fig. by Piotr Nogal):



** an example of uniform disorders which, according to the Author, begin as interchangeably as possible in any of the structures of the "cerebrophthalmic hydraulic loop" in the "vicious circle" mechanism.

We must be aware that an increase in pressure at any segment in the course of the hydraulic loop could mean different risk (in terms of its level and nature) of complications for a particular patient, which is in each case determined by individually variable factors, such as e.g. the shape of anatomical isthmi, variable content of the superior orbital fissure, physico-chemical parameters of blood and aqueous humour 14, condition of the

¹⁴ My attention to the problem of diversification of physico-chemical parameters of the aqueous humour was drawn by **Professor Marek Rękas**. Many of us, including me, who refer to the Professor their most difficult cases of glaucoma patients, believe he is currently one of the best surgical Glaucomatologists and Scientists in this field worldwide, who e.g. intraoperatively collects aqueous humour from posterior chambers of glaucoma patients for laboratory tests, which he told about during his speeches at the Symposium in Ossa near Warsaw, organized by him together with his medical team of the **Ophthalmological Clinic at the Military Institute of Medicine in Szaserów St. in Warsaw**. Prof. Rękas has also been dealing with the issue of pressure diversification in the chambers of the eye for years and has constructed an invasive tonometer of the posterior chamber of the eye.

muscular layer of blood vessels and condition of the iridocorneal angle or resistance of the structures of the bottom of the eye to increased intraocular pressure.

The mechanism of pathological pressure increase in the "cerebrophthalmic hydraulic loop" described by me, which is compatible with Bernoulli's phenomenon referred to the fluid flow through blood vessels associated with the eyeball and dependent on the pupillary block initial in the mechanism with secondary relative intraocular hypertension in the posterior chamber, has been named after the load to which the eye and brain are subjected as a result of this mechanism: "4 lead 4 brain" *** ("four lead for brain" ***)

*** in English: lead ("Pb" in the Mendeleyev periodic table)

"4 lead 4 brain" by Nogal:

1. "Pb - Pupillary Block"



2. "**Pb** - Pressure Behind" (pressure behind the lens and iris; the posterior chamber and vitreous humour chamber)



3. "**Pb** - Phenomenon of Bernoulli" (increase in hydrostatic pressures in the vessels "in front of and behind the eyeball")



4. "**Pb** - Pressure on Brain" (intracranial hypertension caused by \uparrow hydrostatic pressure in the cavernous sinus, which complicates disorders in the circulation of brain fluids; blood and cerebrospinal fluid with numerous secondary neurovascular conflicts)



Pb n° 5... will be the subject of one of the subsequent articles, which is a real eye-opener regarding ophthalmological treatment of patients with systemic disorders distant from the eye!

In order to explain to the reader the physiological rules of fluids circulation between the cavernous sinus of the brain and the eye, I tried to depict dynamically this circulation. That's because we have to be aware that the physical rules concerning the fluid flow dynamics that are compliant with Bernoulli's paradox apply both as universal laws of physics and here. And these are the physical dependencies affecting the eyeball and the brain in pathophysiology that cause, inter alia, selected cases of periodic strabismus, dependent on neurovascular conflicts in anatomical isthmi of the skull. I managed to diagnose this cause of periodic strabismus in several patients, whom I helped non-operatively and effectively.

You will become familiar with the mechanism of periodic strabismus by reading the next publication, to which I already wish to invite you.