AIS: Etiology, Pathogenesis. Facts and Reflections

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Abstract
This article has conceptual character. Authors paid attention to one of the paradoxes of AIS-it's being mono-form in the shape of a 3D deformation at any etiology (polietiology). The explanation of this paradox and its reason was found while performing a mathematical modeling of a 3D deformation. The developed model as "matrix", allowed not only to reestimate a number of known features of real AIS, but also to see the patterns in its development which weren't known earlier. Authors claim that AIS is a compensatory reaction of an organism to the unique circumstance - non-conjugation (non-synchronization) of longitudinal development of a spinal cord and its bone-disc-ligamentous-muscular "sheath". The fact of existence of two types of AIS - typical (lordoscoliosis) and atypical (kyphoscoliosis) serves as the major argument in favor of such conclusion. Speaking of lordoscoliosis, we should know, that the "sheath" has the excess of longitudinal size, and concerning kyphoscoliosis - insufficient longitudinal size. Results of studying an endocrine regulation of a bone formation at patients with both types of AIS allowed the authors to establish features of an osteotropic hormonal profile which is usually directly correlated both with a clinical picture, and with nature of a spine column deformation progress. Causes interest authors interpretation of the melatonin theory of a pathogenesis of AIS. The authors explanation of the origin of phenomenon's EMG is intriguing - they explain it through high electrical activity of muscles on apex frontal curve. In the final part of this article new classification of AIS origin is offered for discussion - hormonal, spinal and central.

Keywords: AIS, Non-conjugation of longitudinal development of a spinal cord and its "sheath", Mathematical modeling

Introduction
In the Preface to the monograph by Aladar Farkas, "Uber Bedingungen und auslosende Momente bei der Skoliosenentstehung", his contemporary von Konrad Alexander Theodor Biezalski (1868-1930) called scoliosis "the orthopedic cross" [1]. Half a century later, Russian vertebrologist Professor Yakov Leont'evich Tziv'an (1920-1987) in his monograph "Scoliosis disease and its treatment" writes "not a single disease in an orthopedic and trauma clinic [...] brings so much disappointment to both the patient and the doctor as scoliosis disease" [2]. The basis of such conclusions was the lack of understanding of the etiology and pathogenesis of the pathological three-plane deformation of the spine arising against the background of the full health of a child.

The need to solve the problem of revealing the laws of the emergence and evolution of idiopathic scoliosis (AIS) as the most common disease of the musculoskeletal system is dictated by the fact that so far in the world "Scoliology" wait-and-see tactics dominate with an expensive outcome in the form of surgical (mechanical) correction of deformity [3]. This position is greatly supported by the conclusion of the American Orthopedic Association, prepared under the guidance of Alfred Rives Shands Jr (1899-1981) in which the unequivocal derivation is "there is no alternative to surgical treatment of scoliosis". However, even the most brilliant result in the work of fellow surgeons does not make the patient healthy [4].

Meanwhile, over the past half century, the inquiring collective mind of the entire community of orthopedists and their colleagues has managed to accumulate plenty of information about AIS.

We believe that the analysis of modern information about this disease already allows one to see a number of patterns in its nature and draw conclusions that bring us closer to creating an effective system for its prevention and early pathogenetic treatment.

Over the past 40 years, large-scale studies of AIS have been conducted at the clinic of the children's orthopedic Center "Ogonyok" (St.-Petersburg, Russia) and methods for its conservative treatment have been developed. As a result, a new view was formulated on the

causes of pathological deformation, objective patterns of the stages of transition of a healthy spinal column to the "scoliosis" status were identified, and "targets" were found, upon exposure to which conservative medical technologies interrupted the pathological process.

It should be emphasized here - if we managed to see scoliosis, known since prehistoric times, from a different angle, this merit belongs to both the Great Greek physician Hippocrates Beta (460-356 BC) and our contemporaries. Sir Isaac Newton (1643-1727) once wrote: "If I saw a little further, it was only because I stood on the shoulders of the Giants" [5].

The Purpose of the Article
We consider it necessary to share with the professional community the results of the discussion of only those basic (due to restrictions on the permissible volume of publication) facts that together create the basis for understanding the nature of AIS and the laws of its evolution. At the same time, we invite to the discussion of the findings, some of which were unexpected for us.

Material and Methods
The article discusses the most common chest-lumbar juvenile idiopathic scoliosis (AIS). To begin with, in it you can see a number of paradoxes.

The main one is so obvious that sometimes it is not even taken into account. This is the conformity of three-dimensional scoliosis deformation (William Adams, 1820-1900) against the background of many reasons for its origin [3, 6]. In 2008, Keith M. Bagnall wrote: "AIS is a common result of several different reasons, and not just one reason, identical in all cases" [7]. In our version it sounds like this:it sounds like this: "AIS is a monoform polietiology process developing with different intensity in each case" [8].

Surprising as it is, the phenomenon described in the previous paragraph completely corresponds to a phenomenon of "a final way", similar to the law of neurophysiology described (1904) in "The Correlation of Reflexes and the Principle of the Common Path" (Ch. S. Sherrington, 1859-1952, Nobel Prize 1932 y.) and named "Sherrington's funnel". This figurative comparison reflects the convergence of several afferent inputs into one anatomically limited efferent channel - motor neuron ("common path") [9].

In other words, with a wide range of primary pathological changes in a wide variety of tissues, organs and systems, they in all cases lead to the only circumstance that initiates the transition of a healthy spinal column to a scoliosis one.

From our point of view, it is precisely ignorance of this circumstance that fully explains the low effectiveness of countering AIS.

There are no processes in nature that the fundamental science mathematics cannot describe. It is only necessary to formulate the problem and find its solution.

Meanwhile, the paradox of AIS conformity should be attributed to the fundamental category, since three-dimensional deformation is possible only in a two-column model, in which both columns have a constant distance between themselves, and their ends are always at the same levels. In such a model, three-dimensional deformation occurs under the only condition - when one column starts changing its longitudinal size. This model is described by the mathematical equation (1) and is shown on FIGURE 1.
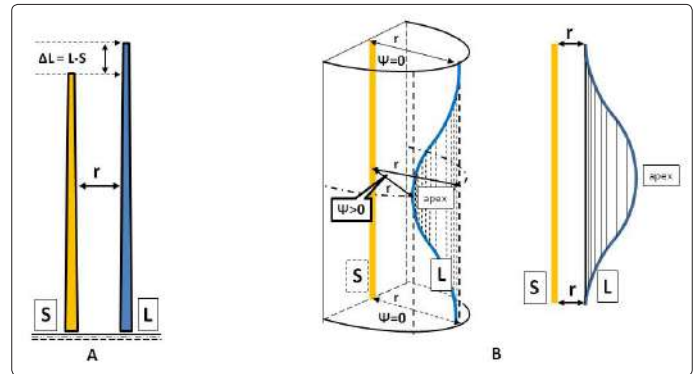

Figure 1A   **Figure** 1B

$$L = S \int_0^1 \left[\sqrt{1 + k(\xi^2 - \xi)^2} \right] d\xi \qquad (1)$$

Figure 1C

Figure 1A: Is a scheme of the two-column model, where: **S** [Short, author note]-is a column that does not change its longitudinal size, **L** [Long, author note]-is a column that changes its longitudinal size, **ΔL=L-S** and r-is distance between **S** and **L**, constant at any level.
Figure 1B: Is a scheme for compensating for different sizes in a two-column model at the expense of two "anti-turns", r-is distance between **L** and **S** (and at the same time-radius of rotation **L** round **S**), **ψ**-is maximum angular span observed when twisting **L** round **S**.
Figure 1C: Is the equation (1) reflects the relationship between the lengths of two parallel segments, where: L and S is the longitudinal size of the columns, $k = 144\gamma^2/S^2$, $\gamma = r\psi$ and $\xi = 2x/S$ (γ - is an accessory parameter, **x** - is a variable for the **x**-axis in figure 1C, **dξ** - is integrable variable).

However, it should be noted that equation (1), which describes **the process of compensating ΔL** due to the "twisting" of a long segment around a short one by an angle **ψ**, is valid only for a perfectly straight model.

However, in the real spine there are sagittal physiological bends in which the initial (primary, natural) differences ±**ΔL** between the corresponding sections of the ventral **L** and dorsal **S** columns are visible (FIGURE 2A). Due to this circumstance, the process of compensating **ΔL** due to twisting cannot be described only by equation (1), which requires equality between **L** and **S**.

The ratio of L^1 and S^1 for "thoracic kyphosis" (for the area of the most frequent localization of scoliosis in humans) is illustrated on FIGURE 2B and is described by equation (2) on FIGURE 2C. This equation allows us to find the value of -**ΔL**, which is necessary to achieve the conditions **L=S** and angle **φ=180°**. In other words, by its content, -ΔL in the "thoracic sagittal bend" is a reserve that does not allow the immediate implementation of the process of compensating for the difference in lengths of **L** and **S** due to twisting
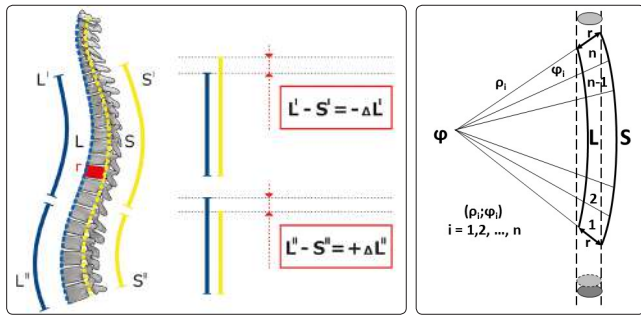
Figure 2A   **Figure** 2B

$$\Delta L = \sum_{i=1}^{n} \varphi_i \left[\sqrt{r_i^2 + \rho_i^2 + \frac{2r_i\rho_i}{\sqrt{1+ctg^2\varphi_i}}} - \rho_i \right] \quad (2)$$

Figure 2C

Figure 3: As shown on the figure, the transition **B → A** leads to the alignment of the heights of the columns, which in the clinical picture corresponds to the formation of a "flat back" syndrome while maintaining parallelism between the frontal axes of the pelvic and shoulder girdles. The **A → C** transition manifests itself in the form of a single-turn twisting of **L** around **S** (in the clinical picture this corresponds to the "torsion of the trunk" syndrome in which there is a violation of parallelism between the frontal axes of the pelvic and shoulder girdles, as well as a steady deviation from the norm of the optical axis). The **C → D** transition appears in the upper part of the model as an oncoming rotation (anti-torsion with the opposite direction), which restores parallelism between the frontal axes of the pelvic and shoulder girdles, as well as the normal direction of the optical axis of the eyes. "*Note*: *Cone-shaped shadow on the figures of all the options are illustrations of the sagittal balance boundaries by J.F. Dubousset* [12]".
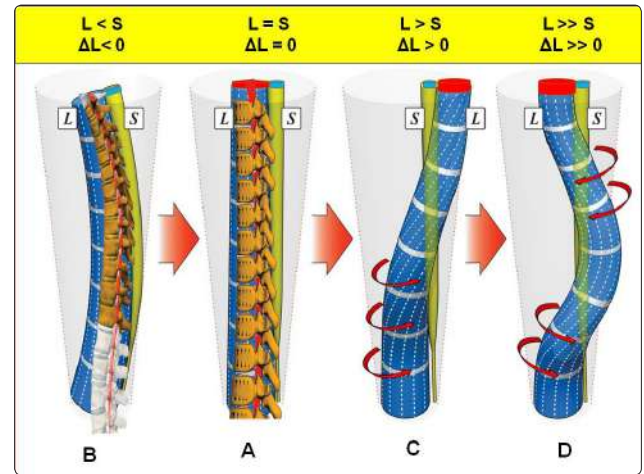
Figure 2A: Is size ratio of ventral L and dorsal S columns in the model with "thoracic kyphosis" and "lumbar lordosis". **Figure 2B:** Is a scheme of a two-column model with "thoracic physiological kyphosis". **Figure 2C:** Is equation (2), which allows you to determine the desired value -ΔL necessary to obtain the straightness of the two-column model where **ΔL=0**, **r**-is the distance between the columns, **n**-is the size of the grid (large enough); ρ(φ) - is the function interpolating the ventral curve **L** on a given grid (at the point φ(ρi)=φi, where φi and ρi are the decomposition of the curve representing one of the parts of **S** into the grid).

Omitting the details of mathematical calculations, we allow ourselves to argue that to achieve the straightness of a two-column model 30-35 cm high with "thoracic kyphosis" of ≈160° (by Cobb), it is enough to add only 1-2 cm to the longitudinal size **L**[1], which are 3-6 %(!) of the height of the model. We note that in order to obtain compensation **ΔL** by twisting a long column around a short one by a significant angle (**ψ**) of 10-20° in accordance with equation (1), a much smaller increase in size **L** is required - only 0,02-0,1%(!) [10, 11].

We note an important fact: an analysis of equation (2) shows that in real conditions with a conceptual vertical position of the model in space in compliance with the requirements of vital sagittal, frontal and horizontal balances, the range of its correct answers has a limit, upon reaching which the compensation **ΔL** takes on absolutely unreal forms [12]. For example - in the form of a screw with one, two and a large number of turns. But this situation, admissible in mathematics, cannot be realized in a real spinal column.

Due to limitations in the size of this article, we will not present the results of a mathematical analysis of the process developing in the lumbar "lordosis" zone (due to the rarity of the "clean" lumbar AIS), but we emphasize that it has quite definite differences.

On FIGURE 3 are presented mathematically justified variants of compensation **ΔL** in a two-column model, in which there is initially a negative value (-ΔL for **L**<**S** in variant B). However, when considering this sequence from right to left, the following conclusions are inevitable: quasi-scoliosis three-dimensional deformation (variant D) is preceded by variant C, which comes from variant B, which reflects the process of using the "reserve" (-ΔL).

Interim conclusion

Thus, the fundamental result of mathematical modeling of quasi-scoliosis 3D deformation was a direct indicator of the main stages in the tragedy that "two actors play on the stage of the most complex segment of the skeleton". It is fair to say that there are publications in the literature (albeit a few!), that take steps to use the mathematical apparatus for an objective description of scoliosis, and the first of them is "Aanmerkingen over de Wanstaltingheden der Ruggengraat" by the Dutch scientist D. van Gesscher (1735-1810) [as presented by Piet JM van Loon in "Recent Advances in Scoliosis", 2012. www.intechopen.com]. However, both it and the messages of recent decades are based on the static characteristics of deformations [13-16]. We did not see any work on mathematical modeling of scoliosis as a dynamic process of deformation of the vertebral complex. Based on the available information about embryology, age-related anatomy, physiology and biomechanics of the vertebral complex, the role of the S column is given to the spinal cord, and the role of the L column is its bone-disc-ligamentous-muscular "sheath" [17-19]. A distinctive feature of our two-column model is its quasi-dynamic character, which is associated with the presence of two variables in children - the longitudinal development of the spinal cord due to the process of "stretching" and the growth of its "sheath" due to the proliferation of osteoblasts in growth plates on the cranial and caudal sides of the vertebral bodies.

In addition, A.I. Kapanji, divides the "sheath" of the spinal cord into two parts - the supporting (vertebral bodies with intervertebral

discs) and functional (vertebral arches with transverse and spinous processes) (FIGURE 4) [19]. The latter serve as levers that provide movement in the spinal motion segment (SMS) or functional spinal unit (FSU) in the biomechanics of the vertebral complex) due to paravertebral mm. transversospinales, which undoubtedly play a role in the process of AIS shaping [20].
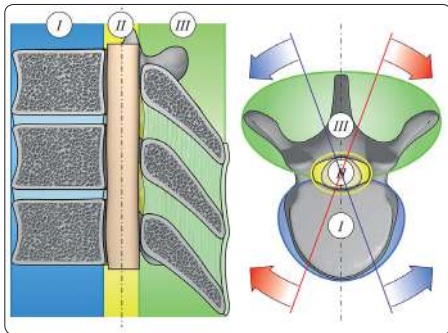
Figure 4: Supporting (I) and functional (III) parts of the bone-disc-ligament-muscular "sheath" (the first column **L**) of the spinal cord (the second column **S**).

A unique characteristic of the spine in Homo erectus is its vertical position. In accordance with the concept developed by J.F. Dubousset [12], a healthy vertebral complex is in an upright position within the "economy cone" (FIGURE 3) with a parallel arrangement of the frontal axes of the shoulder and pelvic girdles and coincidence of the projection of the cranial end with the projection of the caudal end.

Meanwhile, against the background of the above differences in embryogenesis and physiology of the main components of the vertebral complex, they have intimate and far from simple anatomical and functional relationships, the most important goal of which is the joint maintenance of homeostasis of the spine. And, from our point of view, the main macro condition of this homeostasis is a conjugated (or synchronized) longitudinal development of the spinal cord with terminal filament and its bone-disc-ligamentous-muscular "sheath". It should be added here that the fixing ligamentous apparatus of the spinal cord consists of many connective-tissue formations, which, in particular, exclude the longitudinal mobility of an important part of the central nervous system in the spinal canal.

Moreover, as noted above, each of these components (or "columns" L and S), by virtue of its origin, has original features in its longitudinal development. The latter fact suggests that these processes can be non-conjugated (or non-synchronized) for a variety of reasons (from congenital to acquired). As a result, there may appear both an excess and a lack of "sheath" length relative to the longitudinal size of the "spinal cord + terminal filament", which can be called a "medullo-vertebral conflict".

The author of the idea of the key role of this "conflict" is Milan Roth (1923-2006), who in the middle of the 20th century created the "spring-string" AIS model [21]. He believed that a three-plane pathological deformation of the vertebral complex occurs due to a violation of the symmetry of the functioning of the nerve structures in the stretched spinal cord.

Many years have passed since the publication of the works of M. Roth and today there is access to new diagnostic technologies that allow one to return to rethinking previously obtained information, as well as to study some aspects of the functional state of the nervous and endocrine systems. The relevance of the latter is justified by the fact that it is under their control that physiological processes in the vertebral complex exist.

The first fact that became the "key" for understanding the pathogenesis of AIS was the repeated "detection" of two types of "medullo-vertebral conflict", or two variants of the conjugation in the longitudinal development of the spinal cord and its "sheath". The fact of having these options completely correspods to the fundamental principle of variability (dispersion) in biological systems. After all, the vertebral complex is not an inert biological-biomechanical system and deviations of a number of parameters in both directions from "the safety corridor", or from the norm, are quite acceptable in it.

In the clinical and radiological picture, the first appearance manifested itself in the form of "lordoscoliosis" with classic changes in the shape of the spinal column in three planes: lordosis of the "sheath" in the form of "flat back" syndrome, "convex side rotation of the vertebral bodies" and "frontal curvature". The second option was characterized by kyphosis of "the sheath" in the form of "round back" syndrome, "concave side rotation of the vertebral bodies" and "frontal curvature". Simultaneously with us the second type of AIS was described by G.W.D. Armstrong et colleagues [22-26]. In other words, along with "typical AIS" there is a second option - "atypical AIS". Our colleagues led by G.W.D. Armstrong gave this scoliosis the name "non-standard AIS".

Given the differences in the macro anatomy of these two types of AIS, they turned out to be fundamentally different in their evolution (by Hippocrates - "scoliosis is a process!"). In the first case (typical AIS), the whole spectrum of development was observed - from "aggressive and slowly progressive" to "non-progressive". In the second case (atypical AIS), the outcome of three-dimensional deformation never has catastrophic consequences, and the only remaining negative symptom was the persistence of the "round back" syndrome. The maximum value of the frontal curve of the "atypical AIS", which we met in our practice, does not exceed 15° by Cobb. It can be assumed that such a favorable development of this type of AIS to some extent hid the fact of its existence.

It can be justly noted that W. Schulthess in 1902 reported about vertebral bodies concave side rotation, and in a quarter of century A Steindler, confirming the phenomenon, named it as "concave side rotation" (synonyms - "atypical pathological vertebral rotation" by M. Dudin and "non-standard rotation" by G.W.D. Armstrong et coll.) [22-28]. Later, about this variant of pathological rotation wrote J C Risser [29]. The further lack of attention to it can be explained only by the fact that both W. Schulthess and A. Steindler underlined in their works that "concave side rotation" in severe deformations was not observed [28, 29].

A reference to the fact established in the pre-radiological era, "that kyphoscoliosis is not prone to progression in the frontal plane" can be found in the dissertation of M Lüftinger [30]. By the way, the great Hippocrates noted in his writings "back humps" (he did not use the younger term "scoliosis", author note).

The final point in asserting the difference between typical "lordoscoliosis" and atypical "kyphoscoliosis" was based on the results of radionuclide diagnostics of the functional state of bone

tissue in these groups of patients. It turned out that in patients with the classic picture of AIS, osteogenesis is high, and in their peers with "kyphoscoliosis" the intensity of this process was significantly lower [25, 31, 32].

This result was fully correlated with the findings of Monsieur Yves Cotrel (1925-2019) and Madame Ginette Duval Beaupere, Monsieur Jean Felix Dubousset et coll. that "the most indisputable fact in the theory and practice of AIS is the relationship of its occurrence and further evolution with the process of growth of the child" [33-35].

To answer a question about the reasons of difference in a functional condition of a bone tissue in typical and atypical AIS, we chose the main regulators of a bone formation (as bases of the child's growth) - somatotropin (GH) and its functional antagonist - cortisol (Csl), and also calcitonin (Ct) and parathyrin (Pt). The first couple regulates synthesis of an organic matrix of a bone tissue, and the second regulates synthesis of a mineral component. A cumulative picture of their concentration form so-called "osteotropic hormonal profile" (OHP) [23, 26].

Duration of research (1987-1993) allowed to establish nature of development of deformation in each case "de facto" (under observation were 420 children at the age of 9-15 yrs.) and to define average and group indicators of levels of the specified hormones for progressing, the slow-progressive and non-progressive AIS [32, 36]. As a result four OHP options were received (FIGURE 5).
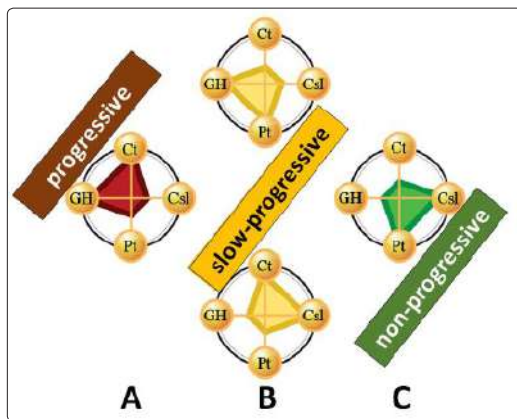
Figure 5: Four fundamental variants of the osteotropic hormonal profile, each of which correlates with the nature of the evolution (progression) of AIS. **A** – is a progressive type of AIS; **B** – slow-progressive type of AIS; **C** – is a non-progressive type of AIS.

At the high level of **GH** and **Ct** only **typical** progression of AIS took place. At the high level of their antagonists **(Csl** and **Pt)** were diagnosed non-progressing **typical** and **atypical** AIS. At the simultaneous raised concentration of "**GH -Pt**" or "**Csl-Ct**", only **typical** AIS with slow-progressing of a frontal curve took place. Let us point out an important detail - the indicators of concentration of the osteotropic hormones gained by us didn't "overstep" the limits of endocrinologic norm.

The provided data are of special interest, because they show "a material basis" for the conclusion by Monsieur Y. Cotrel и Madame Ginette Duval-Beaupere et coll. [33-35]. However, on the other hand,

the "excess" bone formation regulated by osteotropic hormones in a bone spine column cannot have the isolated character because of generalized influence of endocrine system on the whole organism. The fact, that the skeleton of the child with AIS appears higher than of his contemporaries, had been stated by G.G. Epstein as early as in 1981 [37]. Based on anthropological measurements he showed that average height of girls with scoliosis is positively more (p<0,05) than of healthy contemporaries. The similar research, which has been carried out only in 2012 by Zhen Liu et al. led to the same conclusions [38].

On the basis of results of direct studying of the osteotropic hormones and the evidence of their influence on organisms of the growing children we can make the intermediate conclusion - AIS is observed against four main options of an osteotropic hormonal profile which do not exceed, we will highlight, the 'limits of endocrinologic norm'. And each of these options corresponds to the type of evolution of a 3D deformation of a vertebral complex. Behind such conclusion the answer to second main paradoxes of AIS is observed - why not all scoliosis are progressing.

Due to atypical AIS having absolutely good-quality evolution, we will further discuss mainly typical AIS that will allow us to spare publication size.

In reflections about a hormonal factor in a genesis of typical AIS it is impossible to ignore actively discussed "melatonin" hypothesis of a pathogenesis of AIS, the results of experiments of M-J [39, 40]. Thillard went as the basis for it [41-44]. It was established that excision of corpus pineale (epiphysis cerebri) at chickens causes development of quasi-scoliosis deformation in them.

Our opinion on this matter is based on absolutely objective, reflected in numerous publications, fundamental data on the function of corpus pineale, as the main pacemaker in a live organism and its secret - melatonin [41-51]. From these data it follows that melatonin is the major regulator not only of the synthesis of GH and of its already mentioned above antagonist Csl, but also their subsequent biological effect on a bone tissue. Therefore, any deviation, both on absolute concentration of melatonin, and in a circadian cycle of corpus pineale functioning, is simply obliged to be reflected in quality of "collective work" of GH, Csl, Ct and Pt with formation of one of OHP options [45, 48]. Moreover, increased level of melatonin (approximately twice higher than night level in a peripheric blood) in zones of osteoblasts localization and in cells of marrow can be a basis for the assumption of it as about biologically active osteotropic substance [46, 47].

Difficulties of direct diagnostics of the melatonin level in blood of patients with AIS forced us to pay attention to the 3D LocEEG method allowing to study a functional condition of structures of a brain [45, 46, 51]. As justification it is served with that pinealocytes having properties of endocrine cells keep in themselves functions of neurons, i.e. ability to generate and extend nervous impulses [53]. We managed to establish (FIGURE 6) that functioning of corpus pineale as neurohormonal structure, at children with AIS (291 patients at the age of 8-16 years) reliably differs from the picture observed at healthy contemporaries (36 people) [50, 54].
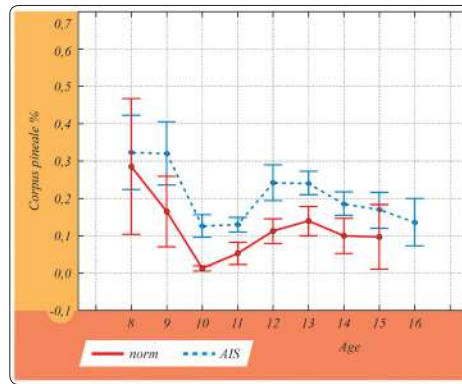
Figure 6: The nature of the activity of the pineal gland in patients with scoliosis in comparison with their healthy peers

As this diagnostics was carried out from 10°° to 12°° AM i.e. when the level of melatonin has to be the smallest, we observed other phenomenon - at children with AIS corpus pineale keeps the functional activity at that time of days when it in norm has to be lowered that it is possible to designate the term "desyncronosis" [45,48,55]. And already it becomes the initiator of the cascade of the subsequent responses for which further maintenance of level of melatonin stops being a necessary condition.

Thus, the major purpose of the directive systems at the growing child becomes regulation of the balance between night intensive synthesis of a bone tissue and day correction of its adequacy. This adequacy provides maintenance of compliance between lengths of a spinal cord and its "sheath" as main physiological condition of a homeostasis for functioning of a vertebral complex. And here the role of melatonin is obvious - at night it frames conditions for intensive "work" on construction of a bone "sheath" of a spinal cord due to stimulation of somatotropin and somatomedin at simultaneous "control" of biological effect of a cortisol. In the morning the situation is reversed and with day decrease of the activity of corpus pineale there comes "freedom" for an adrenal cortisol. However, if we record high bioelectric activity in a zone of an epiphysis at the period of time between 10°° and 12°° AM, we consider that it reflects its hormone-producing function (it coincides with reports of other authors who note normal and even raised content of melatonin in a blood at patients with AIS), it is logical to believe that cortisol did not receive its "freedom" [45, 56]. Indeed, this is already an imbalance sign in osteogenetic process in favor of its synthetic activity. In tubular bones it will lead to simple growth in length. But if we speak about a spine column, unauthorized elongation of bone "sheath" of a spinal cord will lead to stretching of the latter, an excess afferentation of the central structures and then - to start of the whole chain of compensatory reactions.

Pertinent analogy is the avalanche, the reason for which can be a loud sound, a small stone and even a snowflake. The further course of process develops under its own laws according to which its development and consequences do not depend on the reason which caused an avalanche any more. This comparison is very important as it affects the need of differentiation of the starting (etiological) factors for AIS and the pathogenic factors, supporting developments of pathology [57]. We believe that numerous circumstances that qualify as "etiological factors" do not directly initiate AIS themselves. They only create a condition in the form of a non-conjugation (or non-synchronization) between the processes of the longitudinal development of the spinal cord and its "sheath". And only this non-conjugation (or non-synchronization) the one and only condition, can initiate the answer is in the form of the development of monoform three-dimensional deformation of the entire vertebral complex or the transition of a healthy spinal column to the "scoliosis" one.

Meanwhile, it should be noted that the actual stretching of a spinal cord will begin only when the physiological reserves put in a thoracic kyphosis and a lumbar lordosis are used. In a clinical picture it has to be shown in the form of a syndrome of flat-back and in augmentation of an inclination of a pelvis to the front.

We believe that every practicing vertebrologist observes the "flat-back" syndrome rather often. And here lumbar hyperlordosis, though can be met, is much rarer. The rarity of extreme augmentation of a lumbar lordosis during "transition" of a healthy spine column to a "scoliosis" one is explained by a bigger validity of factors of maintenance of optimum vertical position of the person that corresponds to the principle to "an economy cone" by J. Dubousset [12]. And as all observed changes in a form of a vertebral complex throughout this period do not overstep the limits of norm, this stage received the name "preclinical".

The mathematical model as "matrix", allows to claim that in case of development of this conflict situation after use of sagittal reserves, transition to the second compensatory, subclinical stage-a torsion of the supporting column round a spinal cord as variant C on figure 3 will be absolutely natural.

It is important to point out that at this stage (subclinical) mm. transversospinales (mm. Semispinalis, multifidi and rotators) start playing a key role without the participation of which there will be no rotation of vertebrae giving the torsion of a spine column that is necessary for restoration of a normal homeostasis for the most important department of CNS.

Systematic researches of these muscles began in the middle of the XXth century and first of all what settled down in the zone apex of frontal arches [58-66]. Quickly enough found phenomenon - the increased electro activity on convex side at any expression of a symptomatology of AIS, - did not find an explanation in these and other works. We will not stop for extensive discussion on this matter but will only draw a conclusion - juxtaspinal muscles in the zone apex participate in the mechanogenesis AIS, but in what role? We didn't have the answer.

At the end of the XXth century mm. multifidi lumbar were among the studied [67-72]. As a result, it was established (this is our generalized conclusion on the literature data and on conclusions made in our own similar studies, *author note*) that the high electro activity of these muscles on the concave side of the lumbar part of the scoliosis curve appears with the first symptoms of AIS and subsequently highly correlates with the nature of the subsequent evolution of deformation. But what is their role? And this question was not answered as well.

We believe that luck smiled at us when we were able to uncover the essence of these EMG phenomena.
However, before telling about this, a few words about the effect of the reduction of mm. Transversospinales. In the lumbar, most of them are mm. multifidi and normally their traction for the spinous processes of the functional part of the bone-muscular component of the vertebral complex causes two effects [19]. This is the rotation of the subordinate vertebrae in the contralateral direction and, to a lesser extent, the inclination of the spine in the ipsilateral direction. We adhere to the views adopted in world practice. The first - the direction of rotation of the vertebra in the horizontal plane is determined by the side on which its body is displaced. The second - the position of the base (underlying) vertebra, is taken as the starting position or "reference point". When the spine, which is located more cranially, is also involved in the rotation process, it will start from the position that was determined by the previous, already rotated vertebra. The larger the number of vertebrae participating in a unidirectional shift in horizontal measurement, the greater the angle of rotation of the cranial part of the overlying spine [19] (FIGURE 7). Its spiral torsion is the result of successive rotation in several SMS in the spinal column. So, with a small average range of movements in individual SMS (from 5° to 10°), their sum can reach 90°. This can be compared with a spiral staircase in which the upper step is the most turned. We believe that luck smiled upon us when we were able to uncover the essence of these EMG phenomena.
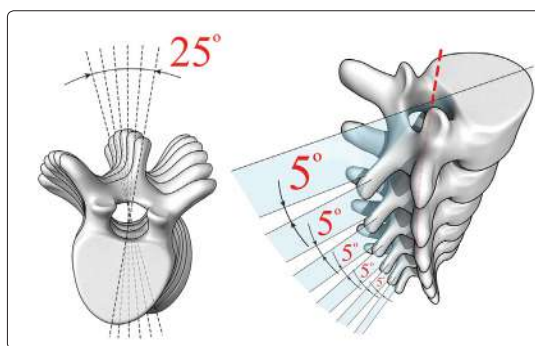
Figure 7: Sequential displacement of the vertebrae in the horizontal plane (rotation), the result of which is the torsion of the vertebral complex (with the effect of a spiral staircase).

Our explanation of the above two EMG phenomena is justified by the results of longitudinal monitoring (2010-2014) of an arbitrarily taken group of 518 children (age 9-15 years, b: g ≈ 40%: 60%).

According to the results of the initial medical examination (May 2010) with the simultaneous computer optical topography of the back, the following subgroups were obtained (Table 1).

Table 1: Statistics of a spine column shape in randomly taken group of the children's population of the city Perm (Russia) in 2010

No of subgroup	Characteristics of subgroup	Amount of children	%%
1	Healthy children /without symptoms of AIS/	45	9
2	Flat back	172	33
3	Round back	62	12
4	Flat back + torsion of the trunk	111	21
5	Round back + torsion of the trunk	30	6
6	AIS up to 10° (by Cobb)	98	19
Total		518	100%

Of particular interest were two subgroups-No. 2 and No. 4. Children from subgroup No. 2 had "clean" flat back syndrome, and in subgroup No. 4 this syndrome was combined with torsion of the trunk. Thus, in their clinical picture, they corresponded to mathematically justified options **A** and **C** on FIGURE 3.

Twenty-six children from these subgroups underwent EMG diagnostics in the juxtaspinal region at the levels of ThIV-ThV, ThVII-ThVIII, ThXII-LI and LIII-LIV.

In subgroup No. 2 (10 children), asymmetric EMG (difference in electrical activity indicators - at least 10%) was registered in only one person and only at the level of LIII-LIV.

In subgroup No. 4 (16 children), the same picture in this zone was already found in 10 people (65%). At the same time, in 12 children (75% of cases) asymmetric electro activity was also recorded at the levels of ThVII-ThVIII and ThXII-L1 [50]. In 4 cases of them, high indicators of muscle electro activity were recorded on the ipsilateral (relative to the lumbar region) side, in 5 cases - on the contralateral side, and in 3 children this correlation was inconclusive. Against this "motley" background, it was noteworthy that in 87.5% of cases (14 people), the direction of the torsion of the trunk (according to the results of optical topography) was fully consistent with the effect of the reduction in mm transversospinalis, i.e. in the opposite direction.

The following diagnostic EMG procedures in the same patients were carried out after 1-3 years. The scope of the article does not allow us to provide detailed data and therefore only the main results will be presented.

From subgroup No. 2, three children "moved" to subgroup No. 4, and among them was a child whose asymmetric electro activity of juxtaspinal muscles in the lumbar region was already observed in 2010. At the same time, all these three patients developed torsion of the torso in the contralateral direction relative to the side with high electro activity of the muscles.

In subgroup No. 4, with the same repeated examinations (after 1-3 years) in 4 children (out of 16, or in 25% of cases), all symptoms of three-plane spinal deformity up to 10° by Cobb were found.

But the most interesting was the fact that in all children with developed AIS, EMG diagnostics in 2010 showed high electrical activity of the lumbar muscles on that side of the spinal column, which after 1-3 years became known as "concave side of the scoliosis arc". At the same time, in all these four patients, high electro activity of the paravertebral muscles (mm. transversospinalis) was stably recorded at the level of the appeared peak of the scoliosis arch. Here we emphasize that in 2010, during the initial medical and instrumental diagnosis in children of subgroups No. 2 and No. 4, signs of the frontal arch were not detected.

We add to the above that the observation of patients coming to our clinic with similar symptoms allowed us to make an interesting observation. So, during an EMG examination of such children at the end of the course of treatment (on average after 45 days), often a high unilateral electro activity in the juxtaspinal region of the lumbar region was recorded already on the contralateral side relative to the initial diagnosis, and in some cases became symmetrical. We believe that this is a reflection of the result of the process of compensating for non-conjugation in the longitudinal development of the spinal cord and its "sheath". If during the treatment process it (non-conjugation) decreased or compensated, then the need to continue the response in the form of "twisting" (the transition of option A to option C on figure 3) loses relevance.

As an interim short discussion, let us say that the content of the above evolution in the clinical picture, corresponding to the transitions options B → A and A → C on figure 3, reflects the firsts pre- and subclinical "steps" on the transition of a healthy spine to a "scoliosis" one. At the same time, it became clear that this process at its beginning is not fatal in nature and can stop (interrupt) at any time due to the mobilization of its own adaptive and compensatory mechanisms of the child's body.

Thus, if we are right, then the content of the period (time of transition of a healthy spine to "scoliosis" one), which K. Bagnall called the "dark zone", ceases to be a mystery, and prevention, i.e. counteraction of AIS at its pre- and subclinical stages becomes real.

But, considering AIS as a process, we must assume that while maintaining the asymmetric electro activity of the muscles of the lumbar zone, complete compensation of the ill-fated non-conjugation at the pre- and at the beginning of the subclinical stage may not take place.

As a result, the torsion of the body in a child is clearly manifested as a clinical manifestation of torsion of the spine. The result of this is a violation of the parallelism of the frontal axes of the pelvic and shoulder girdles which is surely diagnosed at computer optical topography (FIGURE 8).
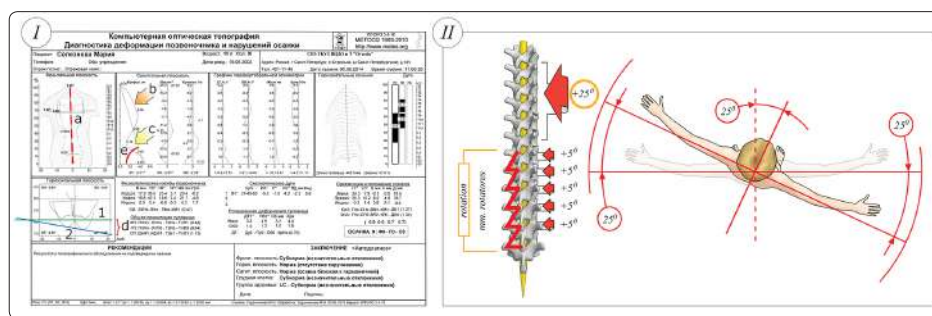
Figure 8: As a result of the asymmetric activity of the paravertebral muscles (mm. rotators, multifidi and semispinalis) in the lumbar region of the vertebral complex is a one-sided torsion of the trunk appears with a simultaneous deviation to the side the optical axis of the human eyes.

However, loss of parallelism in the horizontal dimension of frontal axes of lumbar and humeral girdles is surely reflected in a functional condition of a locomotorium, and also breaks audiovisual perception of environment (in particular - lines of the horizon). P-M. Gagey and B. Weber wrote that the ophthalmologist of J-B Baron found "strong tonic postural asymmetry of juxtaspinal muscles" as result of the "section of tendons of oculomotor muscles causing a deviation of axes of eyes that is less than 4°" [73-76]. This directly proves, what even the minimum deviation of visual axes already causes the necessity of its correction or compensation. Moreover, J-B. Baron directly indicates a place of realization of the compensatory mechanism - a spine column.

**Interim Short Discussion**

We believe that this phenomenon will inevitably take place in full during a subclinical stage, since the described violation of parallelism of the frontal axes of the pelvic and shoulder girdles will change the direction of the optical axis.

In other words, the twisting of the spine, starting as a subclinical stage of compensation for the non-associative longitudinal development of the spinal cord and its "sheath", will undoubtedly reach 4°. This fact, we reflect further, should cause the described J-B. Baron the phenomenon in the Supraspinal muscles as an adaptive and compensatory response in order to compensate for the deviation of the axis of vision [74-76]. It turns out that the previous compensation for non-conjugation due to the torsion of the body caused the need to compensate for its result already! Torsion of the spine required it's detorsion.

The detorsion process has two solutions, but in both of them it is performed with the same mm. transversospinales on the opposite side. The first solution is the complete elimination of torsion due to the symmetrically positioned mm. transversospinales and if this leads to the elimination of the non-conjugation between the spinal cord and its "sheath" the shape of the spine will return to normal. The second solution is local detorsion in the cranial zone of the spine, which will lead to the formation of an anti-turn from the overlying vertebrae to the contralateral side (relative to the direction of primary torsion) (FIGURE 10, A, B).
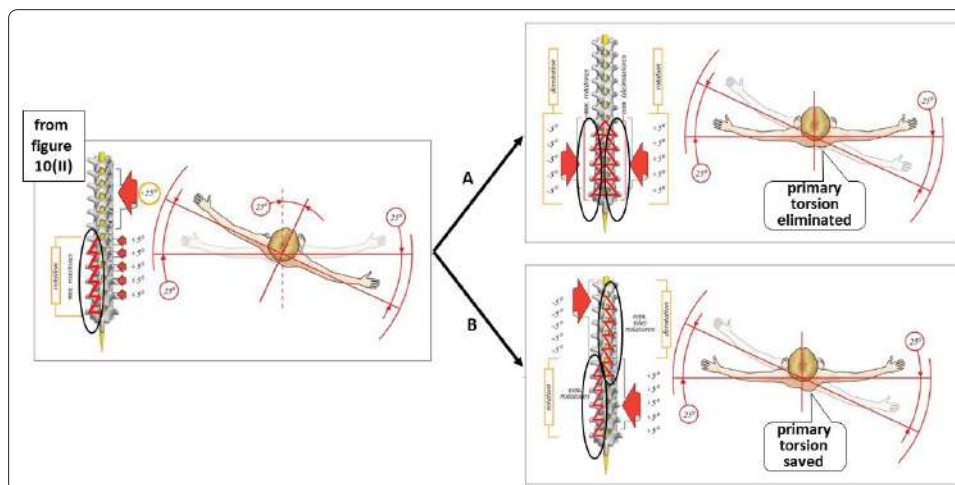
Figure 9: Two options for primary torsion compensation. **A** - due to the activation of symmetrically located countralateral paravetebral muscles, the result of which is the complete elimination of the torsion of the trunk with the restoration of the normal shape of the spine and the position of the optical axis of the eyes. **B** - due to the contralateral paravertebral muscles located above and serving the thoracic vertebral complex. As a result of their "work" an anti-turn is formed, which restores the correct position of the optical axis, but at the same time, together with the primary turn, it forms a curvature of the supporting column consisting of vertebral bodies and intervertebral discs.
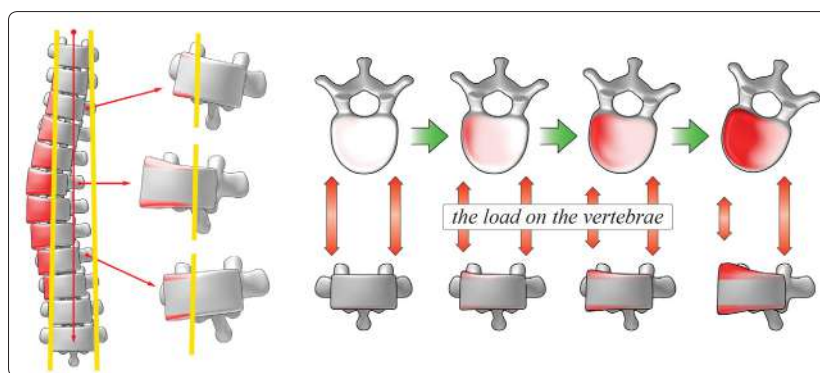
Figure 10: Uneven load on the right and left sides of the vertebral bodies creates the conditions for the implementation of the Hueter-Volkmann effect and the formation of wedges in them

The normal functional anatomy of these muscles is such that on each pr. spinosus simultaneously end mm rotatores (from the pr. transversus of the first underlying vertebra), mm. multifidi (from pr. transversus of the 3-4th underlying vertebrae), as well as mm semispinales (from pr. transversus of the 5-6th underlying vertebrae). Thus, in order to remove any vertebra from the primary rotation position, the muscles that are attached to the pr. transverses of 2-6 vertebrae below must contract. This fully explains the already mentioned EMG phenomenon - the high electroactivity of the muscles in the juxtspinal region on the convex side of the apex of the scoliotic curve. It is there that the

contraction of mm. rotatores, multifidi et semispinales occurs, which, unlike the muscles of the caudal zone, play the role of "derotators". The anti-turn of a spine column, the same in size, becomes a result of a detorsion in a cranial zone and together with caudal (remained from primary torsion) they change a form of the carrying column - there emerges a frontal curve. Thus, the frontal component, finishing the formation of a 3D deformation is added to the changes of a vertebral complex in the sagittal and horizontal dimensions which were available at preclinical and subclinical stages. It gives the grounds to call the last stage "clinical".

We bind further development of AIS with features of anatomy of a spine column. So, at convex side rotation (typical AIS) the carrying column is displaced from a vertical aside and there happens its "disclosure as a fan". Only lig. Longitudinal in front of the intervertebral symphysia and art-s zygapophysiales resist to this process. In case of continuation of the vertebral bodies' growth in height, such counteraction for further "disclosure" can be not sufficient and it will accrue. One more adverse factor - Hueter-Volkmann effect, to which one I A Stokes has been trying to draw everybody's attention to for a long time [77, 78].

However, we should note - we do not agree with the respectful author that asymmetric growth of bodies of vertebrae is the primary factor forming scoliosis in the normal, evenly loaded vertical spine column. Indeed, the conditions for such growth necessarily appear already at the very beginning of the "clinical" stage, when the strict verticality of the spinal column is violated. Asymmetry of a load on cranial and caudal surfaces of bodies of vertebrae (on condition of activity conservation their growth zones) will provide realization of Hueter-Volkmann effect and as a result will lead to "vicious circle" - the more asymmetry of a vertical load, the more it becomes wedge-shaped, the more it is wedge-shaped, the more deformation it causes, the more deformation is caused, the more asymmetry (FIGURE 10) is observed.

At the second type of AIS (atypical or non-standard) with concave side rotation, the supporting column of a spine remains in vertical position and the spinal cord located in the vertebral channel twists round it. In such situation "the effect of a fan" is observed in dorsal, functional part which has no ability for longitudinal growth. It means that process does not gain further development and AIS with this radiological picture does not progress (in the frontal dimension) [10]. Moreover, position of bodies of vertebrae is such that due to the same Hueter-Volkmann effect their growth will restrain and in a clinical picture the sagittal 3D deformation component will start prevailing (round-back).

Conclusion
We hope that our analysis of the above modern information about AIS (their quantity and quality can be compared with a set of puzzle parts from which it is necessary to add the whole picture, author note) was quite logical, and the conclusions are convincing. Indeed, today the amount of information about this very studied lesion of the children's spinal column has reached that critical mass, which is rather enough to get as close as possible to the disclosure of the essence of this disease, since the relevance of identifying "targets" for effective prevention and treatment of a crippling child's spinal column deformity is not only medical, but also financial reasoning. The latter is illustrated by the fact that the absence of a system for predicting the evolution of scoliosis in specific cases forces one to spend equal resources on combating both progressive and non-progressive deformities. And the effectiveness of such costs (read "the effectiveness of conservative treatment", *author note*) remains quite low, as statistics indicate - every tenth patient has spinal deformity which reaches critical values and, in opposition to it, doctors follow the recommendations of the American Orthopedic Association [4]. But, as was already noted in the Introduction, does expensive surgical correction return a person to a healthy state and does it give a high quality of life?

It follows that an understanding of the etiology and pathogenesis of AIS is not a problem only of academic orthopedic science.

The First One: Relying on the knowledge and achievements of the world "Scoliology" and having "behind the back" our own multifaceted studies of various aspects of AIS, we offer for discussion our point of view on its pathogenesis (FIGURE 11)
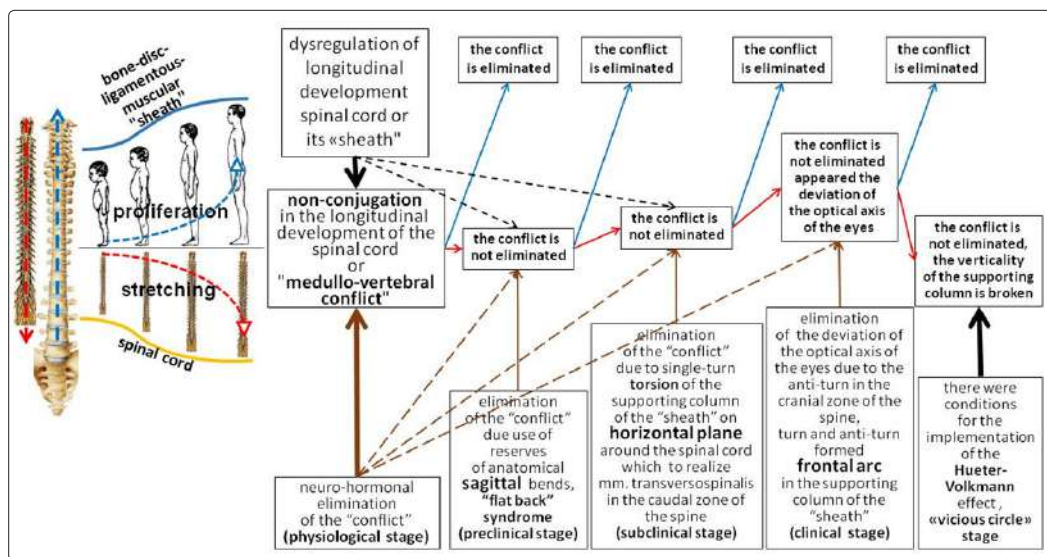
Figure 11: Scheme of the main stages of the pathogenesis of the transition of a healthy spinal column to the "scoliotic" one

The Second One: Considering Non-Conjugation of longitudinal growth of a spinal cord and its "sheath" the key circumstance in initiation of 3D deformation development, we offer versions of its origin for discussion, which become a basis for our classification of AIS:

1) Hormonal Non-Conjugation (Hormonal AIS): All options (from congenital to acquire) of organ and functional disturbances in endocrine glands, including APUD system leading to an intensification or suppression of longitudinal body growth of a bone spine column (at absolute norm in an anatomo-functional condition of a spinal cord).

At hormone dependent excess (concerning length of a spinal cord) longitudinal growth of bone-disc-ligamentous-muscular "sheath" - therefore as compensation a typical AIS develops.

At hormone dependent insufficiency (concerning length of a spinal cord) longitudinal growth of bone-disc-ligamentous-muscular "sheath" - therefore as compensation an atypical AIS develops.

2) Spinal Non-Conjugation (Spinal AIS): All options (from congenital to acquire) of organ and functional disturbances in a condition of a spinal cord leading to deviations in its longitudinal growth are the cornerstone of the spinal non-conjugation (at the age norm in a hormonal regulation of longitudinal growth of its bone-disc-ligamentous-muscular "sheath").

With an insufficient longitudinal growth of a spinal cord there evolves its shorting concerning "sheath" and as a compensation a typical AIS develops.

With an excess longitudinal growth of a spinal cord there evolves its elongation concerning "sheath" and as a compensation an atypical AIS develops.

3) Central Non-Conjugation (Central AIS): Disturbance or distortion of information transfer at the level of thalamus-hypothalamus-hypophysis is the cornerstone of the central non-conjugation These structures of a brain carry out coordination of functioning of nervous and endocrine systems in the closest interaction with corpus pineale (first of all - through suprachiasmatic nucleus of hypothalamus (SCN)). And all of them, as well as other organs and tissues, "have the right" to the congenital and acquired anatomic-functional disorders. In that case there can be functional deviations in the specified structures influencing nature of relationship in longitudinal development of a spinal cord and its "sheath" which, in turn, will demand the compensatory reaction in the form of typical or atypical AIS.

The Third One: The proposed new etiological classification of the key circumstance initiating AIS (**Non-Conjugation** of the longitudinal development of the spinal cord and its "sheath") simultaneously indicates "targets" for combating this lesion of the spinal column. Our experience (for more than twenty years, author note) shows that the use of a specific method of drug- and electrotherapeutic correction of osteotropic hormonal profile (OHP) allows one to confidently achieve interruption of the progressive evolution of scoliosis, and in combination with other edical technologies (in particular - with the polarization of the brain and/or spinal cord) to receive even regress of deformation.

However, it should be noted that while conservative treatment in the above direction is faced with a technology deficiency of percutaneous influence on the processes of longitudinal development of the spinal cord and its bone-disc-ligamentous-muscular "sheath".

Therefore, in the finale we express the hope that this publication will contribute to the attraction of new "smart heads" that will go further than us [79].

Acknowledgments

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