## Materials of Conferences

## THE SPIRIT-PROCAINE BLOCKADES IN THE TREATMENT OF THE VERTEBRAL ARTERY SYNDROME

Khachatryan A.M., Sizgunov D.S.
Saratov state medical university, department of
hospital surgery
Saratov, Russia

The irritative and reflective spasm of vertebral arteries (VA), besides extravascular compression, plays a big role in the development of the spondylogenous vertebral-basilar arterial insufficiency (VBI).

We have investigated 45 patients with VBI. During the X-rays examination all the patients had got degenerative changes in cervical spine, as in vertebras, so in intervertebral joints and disks.

Duplex ultrasound investigation found extravascular compression of vertebral arteries — in 12 cases two-sided, in 23 - unilateral. The levels of compression were identified with data of the X-rays examination of the cervical spine. The spasm of VA without compression took place in 10 cases. Transcranial ultrasound investigation had found the decrease of linear blood circulation rate (LCR) in VA, also in the basilar arteries (BA) in the most cases. There were the increase of the resistant index (RI) in these arteries in all the cases, which is the objective deponent of the spasm. We have also revealed positional dependence - while turning head to the contralateral side the LCRs in the injured VAs were decreased by  $34,5\pm3,3\%$  from the initial, and in the BA – by 28.9±2,7%; simultaneously were increased RIs — by 0,08 from the initial significations (on the average).

The procaine blockades (PB) of the periarterial sympathetic plexus at the level of the third segment of VA (S.Novocaini 2% - 3ml) were performed to all 45 patients. For 15 of them (with damage of the both VAs) were made bilateral blockades, for the remaining — at the injured side. After 7 days were made periarterial alcoholizations (PAA) for all the patients at the same level (30° ethyl alcohol). The neurological and ultrasound examination was repeated in 3, 72 hours after PB and in 3, 72 hours and on the tenth day after PAA.

In the nearest period after PB the improvement of the condition, the decrease of the clinical signs of VBI and positional dependence were noticed in the most cases(66,7%). On the whole, good and excellent nearest results had got 30 among 45 patients. The duration of the effect of PBs was ranged from 5 to 72 hours.

The positive dynamics in neurological condition after PAA on the whole is similar with the early therapeutic effect of PBs. The regression of the symptoms had come in the more number of the patients than after PB. Besides, the therapeutic efficiency of the PAAs was more steady than after the PBs — sig-

nificant improvement of the clinical condition after 72 hours was noticed in 36 cases(80%).

At the end of the hospitalization (10<sup>th</sup> – 12<sup>th</sup> day after PAA) 12 patients had got excellent, 21 – good and 7 patients – satisfactory results of the therapy.

The clinical improvement was correspond to the ultrasound data. The LCR has increased in comparison with the initial ones from 35,2 to 42% in VAs, and from 22,4 to 52% in BAs, 16 patients had got normal indexes. Normal indexes of RI were noticed in the most cases, the positional dependence has decreased significantly. The reduction of the interhemispherical asymmetry of the circulation took place in all the cases with one-sided defeat of the VAs.

The application of the spirit-procaine blockades of VA is effective and pathogenically justified method of treatment of the VBI caused by vertebral pathology.

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## THE BIOLOGY OF THYMOSIN PEPTIDES

Parakhonsky A.P. Kuban medical university Krasnodar, Russia

The thymosins are a family of hormonal-like peptides which in combination with cytokines, T-cells, B cells, dendritic cells, and macrophages, help to provide an immune umbrella for combating pathogenes, destroying malignant cells and regulating wound healing and angiogenesis. Thymic derived peptides isolated from thymosin fraction 5 also play a more general physiological role and have been found to influence a number of endocrine and neuroendocrine pathways. Biological response modifiers such as thymosin- $\alpha_1$  (T $\alpha_1$ ), are produced in significant quantities within the thymus whereas other for example, thymosin- $\beta_4$  (T $\beta_4$ ), the major actin sequestering peptide in cells are more ubiquitous in nature and are found in highest concentrations in blood platelets, neutrophils, macrophages and a wide variety of other cell types.

Recent studies have established that Toil can block in a time and dose dependent fashion glucocorticoid (GC) induced apoptosis of immature thymocytes. Apoptosis of developing thymocytes is a crucial process in the development of T-cell immunity. The life and death of thymocytes (as well as other cells), is a crucial balance of microenvironmental and intracellular signaling. Apoptosis of thymocytes is influenced by interaction between developing thymocytes and the microenvironment of the thymus. This finding may

further help to characterize other potential therapeutic applications for  $T\alpha_1$ . Current studies demonstrate the potential for  $T\alpha_1$  in modulating the effects of GC induced immunosuppression and suppression of thymic function. Results from this study and previous studies suggest that  $T\alpha_1$  can potentially protect non-selected thymocytes from GC induced depletion within the thymus thus allowing for increased time for selection and production of new thymocytes.

Clinically,  $T\alpha_1$ , is now approved in 21 countries and has been utilized for the treatment of patients with cancer and immune deficiency disorders including AIDS, chronic hepatitis B (HepB), and hepatitis C (HepC) and as an adjuvant to enhance the efficacy of vaccines in the elderly and in immunocompromised patients.  $T\alpha_1$  is active as a monotherapy for HepB and in combination with interferon, in HepC. It has a very good safety profile.  $T\beta_4$  was first characterized by its ability to stimulate the expression of terminal deoxynucleotidyl transferase, a non-template directed DNA polymerase in bone marrow stem cells and to inhibit macrophage migration. Known, that it is the major actin sequestering peptide in normal mammalian cells and plays an important role in the remodeling and healing of tissues. Tβ<sub>4</sub> has been found to accelerate wound healing and angiogenesis in a variety of in vitro and in vivo models. Tβ<sub>4</sub> represents a new class of wound healing compound. It is not a growth factor or cytokine but rather exhibits a number of physiological properties which include its ability to sequester and regulate actin, its potent chemotactic properties (specifically for endothelial cells), and its capability to down regulate a number of inflammatory cytokines that are present in chronic wounds.

Over the past few years, remarkable progress has been made in the biochemical and clinical characterization of many of the major isoforms of  $T\beta_4$  in both normal and abnormal cells. To date, about 20 isoforms of  $T\beta_4$  have been identified. Using microarray analysis, it has now been established that a number of  $\beta$  thymosins are regulated in a variety of disease states including cancer. Studies are currently underway to determine whether characterization of specific  $\beta$ -thymosins including an isoform of  $T\beta_4$  not found in normal tissue will be useful in helping to diagnose specific disease entities and to develop new therapeutics for treatment.

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## THE NEUROIMMUNE BIOLOGY – CURRENT STATUS AND FUTURE POTENTIAL

Parakhonsky A.P. Kuban medical university Krasnodar, Russia

There is a strong popular belief in midbody interaction since prehistoric times. Pathologists noted first that the size of the thymus was profoundly influenced by emotional events and by neuroendocrine abnormalities. Hans Selye discovered (1936) that the hypothalamus-pituitary-adrenal axis was activated by diverse "nocuous" stimuli, which lead to a rapid involution of the thymus. He called the agents eliciting this phenomenon "stress". Selye concluded that stress induced a "general adaptation syndrome", which elevated the resistance of the animal to diverse insult. Hypothalamic lesions were shown to prevent anaphylactic death in guinea pigs in 1949 by Szentivanyi and colleagues. This demonstrated the dominant regulatory power of the nervous system over immune reactions. Korneva and Kai (1965) made similar observations were made in various animal species. Jancso and co-workers (1964) discovered the neural regulation of inflammation. These fundamental discoveries were not followed by intensive research activity. Progress has been slow because of the lack of basic knowledge and because of the immense technical difficulties encountered by investigators of this area.

In the seventies a handful of laboratories started to re-examine various aspects of neuroimmune-interaction. It was established that pituitary hormones have the capacity to stimulate, inhibit and modulate immune responses. Placental and pituitary hormones were also shown to be involved in immune system development and in the maintenance of immunocompetence (Berczi et al.). The innervation of lymphoid organs and cells was demonstrated. Neurotransmitters and neuropeptides were shown to be important immunomodulators. (Felten et al., Bienenstock et al.) Gradually immune derived cytokines were shown to deliver feedback signals towards the neuroendocrine system (Wenmacher, Besedovsky et al., Goldstein et al.). Compelling evidence was produced, indicating that immune reactions may be conditioned in the classical paylovian sense and that emotions affect immune function (Ader et al., Bienenstock et al.). Evidence is increasing rapidly for the physiological role of cytokines and of immunocytes in the function of various organs and tissues, and in reproduction. It is also becoming obvious that Selye's general adaptation syndrome corresponds to the acute phase response. This is a multi-faceted and highly coordinated systemic defence reaction, which involves the conversion of the immune system from a specific, adaptive mode of reactivity to a rapidly amplifiable polyspecific reaction mediated by natural immune mechanisms. Immunological (poly)specificity is assured by profoundly