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THE THERAPY OF THE ADVANCED RENAL CELL CARCINOMA – NEW AGENTS AND STRATEGIES

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In the last 30 years advanced renal cell carcinoma (RCC) had a dismal prognosis with the only available systemic agents being interferon and interleukin-2. Occasional durable responses were seen with high dose interleukin-2, but the toxicity of these agents was very expressive.

Over the past few years, several novel targeted agents have received approval in the USA and Europe for advanced RCC. These include sorafenib, sunitinib, temsirolimus, bevacizumab and everolimus. Temsirolimus is primarily indicated for highrisk disease on the Motzer prognostic index. Both sorafenib and sunitinib are available for first-line therapy of advanced RCC, however, the clinical data suggests that sunitinib is the most commonly selected systemic agent for first line therapy of advanced RCC.

Several novel agents have recently completed phase III trials in advanced RCC and received the approval by the FDA and in Europe. These include bevacizumab, which in combination with interferon-alpha 2a demonstrated a significant increase in progression-free survival (PFS) and objective response rate compared to interferon-alpha 2a plus placebo.

Another novel agent expected to receive FDA approval for RCC in the near future is pazopanib. This is another tyrosine kinase inhibitor (TKI) that targets VEGFR-3, platelet-derived

growth factor receptor (PDGFR) alpha and beta as well as c-kit. Phase II studies have demonstrated an objective response rate of 27%. A phase III trial comparing pazopanib to placebo in patients with locally advanced or metastatic RCC, who have received 1 prior systemic therapy that did NOT include anti-angiogenic agents, has been completed and is expected to be presented in the near future.

Finally, everolimus, the first oral m-TOR inhibitor has completed a phase III trial in which everolimus was compared to placebo in patients whose disease had progressed on sunitinib, sorafenib or both. Progression-free survival benefit was seen in all 3 Motzer risk groups.

Actually physicians treating patients with advanced renal cell carcinoma have an expanding array of therapeutic choices to consider. How these various agents are the sequence or combination of these various agents are may significantly affect duration of survival for the patients. Not all of these agents can be combined safely and only evidence based combinations should be considered in a non-clinical trial situation. Participation in clinical trials will be of even greater importance as efforts to determine the most effective combinations and sequential use of these novel agents are explored.

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YKL-40 IN SERA OF BREAST TUMOR PATIENTS

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Objectives: YKL-40, also known as human cartilage glycoprotein 39, is a member of the B•Bmammalian chitinase-like protein's, but lacking of chitinase activity. Increased variations in serum concentrations are associated with inflammatory processes and several types of cancer. In this study we evaluated serum YKL-40 levels in healthy controls and in women with benign and malignant breast tumors

Methods: YKL-40 serum levels were measured by enzymelinked immunosorbent assay - ELISA in 32 patients. The effect of the various factors was analyzed using correlation and regression analyses simultaneously determining the size and direction of correlation. The level of statistical significance of null hypothesis was P<0.05.

Results: Our study showedthat serum YKL-40 level in breast carcinoma was significantly higher than the concentration in healthy controls (p<0.01). The changes in protein levels were higher than 25%. Serum YKL-40 increased with age (rxy=0.46). The correlation between glycoprotein quantity and age was positive, but feeble.

Conclusion: This investigation is first in Bulgaria to demonstrate significantly elevated serum YKL-40 level in breast carcinoma compared to women with benign breast tumors and healthy controls. Longitudinal studies are needed to confirm YKL-40 as a potential and reliable biomarker.

The study is supported by grants No-1/2009 and No-5/2008 from Medical University - Plovdiv.

YKL-40- A NEW DIAGNOSTIC BIOMARKER FOR BENIGN BREAST DISEASES AND BREAST CANCER

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Benign breast diseases encompass a wide spectrum of lesions, which raise a lot of questions about their classification, diagnosis, prognosis and surgical treatment. The aim of this study is to measure the serum level of YKL-40 in cases of different groups of benign breast diseases, to compare it to the level of healthy women as well as to those with breast cancer and to examine its tissue expression after surgical treatment. We use it as a diagnostic marker and as a criterion for differential diagnosis.

Forty nine (49) patients with benign breast diseases and

twenty (20) patients with breast cancer were examined. All of them had their serum level of YKL-40 measured preoperatively and its tissue expression examined immunohystochemically after the surgical intervention. There were significant differences in both concentration and tissue expression of this marker in patients with different groups of benign breast diseases and breast cancer. YKL-40 can be an important biomarker in the diagnosis and differential diagnosis of breast diseases.

Key words: breast, YKL-40, benign diseases, biomarker

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INVESTIGATION OF SOME IMMUNOHYSTOCHEMICAL INDICATORS IN BENIGN SURGICAL DISEASES OF THE BREAST

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Benign breast diseases are a big group of lesions affecting women of all ages from puberty to old age. Some of them have the potential to become malignant in a different period of time. In this article we investigate the immunohystochemical expression of E-kadherin and p-63 in patients who underwent surgery in our clinic. The lesions were of different subgroups of benign diseases. The expressions of the above mentioned markers can be of use as a criterion for early diagnosis and surgical treatment of the lesions before they have eventually become malignant. We investigated 45 women of the three subtypes of benign diseases – nonproliferative, proliferative without atypia and

proliferative with atypia (the so called premalignant diseases). We compared the expression of E-kadherin and p-63 with their expression in patients with breast cancer and a control group of women. We used the results of immunohystochemical analysis of these markers, together with other clinical features, as a criterion for dividing the patients in groups of high-risk and no-risk of subsequent breast cancer.

We believe that the analysis of the expression of E-kadherin and p-63 will contribute to earlier diagnosis of breast cancer and its timely surgical treatment.

Key words: E-kadherin, p-63, benign breast diseases

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PERITONEAL METASTASES IN COLORECTAL CANCER

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The peritoneal surface is affected in 10%-15% (synchronous metastases) of the patients with colorectal cancer and in

20%-25% of the patients with recurrence (metachronous metastases). (1) The peritoneal metastases take the second

place after the hepatic metastases from colorectal cancer. The peritoneal metastases develop after direct implantation of cancer cells by one of the following mechanisms: 1) spontaneous intraperitoneal dissemination of cancer cells from T4 colorectal cancer invasion of the serosa; 2) extravasation of cancer cells after colon perforation due to obstructing cancer 3) iatrogenic cancer perforation caused by resection of the colon; 4) dissemination of cancer cells through the descending venous and lymph vessels during

resection of the colon. In conclusion, the standard approach in the treatment of patients with peritoneal metastases is the systematic chemotherapy. Nevertheless there is evidence that the patients with aggressive cancer disease benefit from aggressive cytoreductive surgery and intraperitoneal chemotherapy. Furthermore additional studies are needed to establish the optimal use of contemporary aggressive methods in the treatment of peritoneal carcinomatosis.

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DO WE NEED A CHANGE IN STRATEGY FOR TREATMENT OF IV STAGE COLO-RECTAL CANCER

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Introduction: In the past decades the improvement of surgical technologies and modern adjuvant therapy lead to revolutionary changes in multimodal approach in treatment of liver metastatic lesions from colorectal cancer. The achieved results are encouraging and the surgeons receive the opportunity for individual approach to every patient for maximizing the outcome. "Which approach is suitable for which patient?" is already not a disputable question. The classic surgical approach is consist of surgical treatment of the primary tumor at first place and after that treatment of liver metastases is commenced. Despite of that in many patients the metastatic process progresses and obstructs the sanitation of the primary lesion. Upon this some authors create strategy, which includes as first step powerful neo-

adjuvant chemotherapy, as second step is commenced resection of the metastases and as last level – resection of the primary tumor. According to some authors this inverted "approach" in the treatment of colorectal cancer leads to better results in respectability and survival rate. This approach is indicated in patients with non-obstructive tumors. In the basis of this "inverted approach" stays the opinion that the patient dies from the complications, connected with metastatic disease.

Conclusion: The treatment of liver metastases from colorectal cancer is a dynamic and continuing process. The multimodal approach allows building individual strategy in the treatment every single patient.

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A CASE OF ENCAPSULATED NEUROMA

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Palisaded and encapsulated neuroma is firstly described by Reed et al. 1972.

This uncommon tumor, usually presents as a solitary mass on the face of middle-aged patients. It has a fine capsule fascicles of neurons interwine together. There is palisading arrangement of the niclei.

We present a case with Palisaded and encapsulated neuroma in 56 years old male, with nonpainful lesions on the basis of the nose - right side. In three months it enlarged its diameter. No other serious systemic diseases are announced.

ETIOLOGY AND SYMPTOMATOLOGY OF SKIN PSEUDOLYMPHOMA

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Cutaneous pseudolymphomas are reactive lymphocytic proliferations that appear in the skin and resemble a malignant lymphoma.

Most of the pseudolymphomas are caused by infections with B. Burgdorferi, others include tattoo reactions, immunizations or allergens desensibilization injections and infection with herpes simplex and zoster.

The most common clinical manifestations are: a single large nodule or solitary and multiple lessions. They are sharply bordered, soft, redish, dome- shaped and covered by thinned skin.

The sites of predilection are the ear lobes, nape, nipple and areola, axillae, scrotum and dorsum of the foot.

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LOCALIZED FORM OF LYMPHOMATOID PAPULOSIS, EVALUATING IN T-CELL LYMPHOM.

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Lymphomatoid papulosis is presented by spontaneously regressing cutaneous infiltrates, that microscopically resemble a lymphomas and may evolve into Hodgkin or non-Hodgkin malignant lymphoma.

We present a case of Lymphomatoid papulosis in a 64 years old male, who complains from reddish non painful papules,

localized symmetrically on the back and lateral zone of the legs. The patient was treated for 10 weeks with low dose of methotrexat (15 mg per week) with good clinical result.

One year after treatment interruption the same patient had a similar clinical changes and hystochemical signs for development of T-cell lymphoma.

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POSSIBILITIES FOR DRUG-INDUCED PSEUDOLYMPHOMA

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Lymphoproliferative infiltrates could be seen in several skin diseases but they are very characteristic of cutaneous pseudolymphoma, which can mimic both clinically and histopathologically cutaneous malignant pseudolymphoma. A big problem for the clinicians is the differential diagnosis between cutaneous pseudolymphoma and malignant cutaneous lymphomas, as well as possibility for transformation of cutaneous pseudolymphoma into

malignant lymphomas.

Wide spectrum of medicaments could cause appearance of cutaneous pseudolymphoma. Some of them are: anticonvulsants, ACE inhibitors, neuroleptics and others. Many of them are responsible for a development of erythrodemia, simulating Sezary syndrome with peripheral blood changes.

ETIOLOGY AND SYMPTOMATOLOGY OF CUTANEOUS PSEUDOLYMHOMAS

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The cutaneous pseudolymphomas are benign reactive proliferations of the lymphocytes in the skin, that can resemble malignant lymphomas. They can be performed by gathering of lymphocytes as an answer to different stimuli (infections, medicaments, insect- bite reaction).

They are heterogeneous group of dermatoses, clinically variated from tumor like nodules to squamous- cell infiltrates. Depending on the kind of the cellular infiltrate, cutaneous

pseudolymphomas are divided into 2 main groups:

- B-cell pseudolymphomas
- T-cell pseudolymphomas

Most common clinical appearance of cutaneous pseudolymphomas is solitary lesions forming plaques and tumors.

Mostly affected areas are: head, ears, nose, but in children

- around the mammillae.

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CONTEMPORARY CLASSIFICATION OF THE CUTANEOUS PSEUDOLYMPHOMAS

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Systematizing of different diseases and skin disorders is quite difficult. Different authors do that having in mind numerous criteria. Pseudolymphomas are reactive lymphocytic proliferations that appear in the skin and resemble a malignant lymphoma.

There are different classifications of the cutaneous pseudolymphomas. The widest is that, which differs them into 6 groups, but mostly used is that, which is based on clinical and morphological criteria.

According to the last classification (Rijlaarsdam & Willemze), they divide into:

- -cutaneous T-cell pseudolymphomas
- cutaneous B-cell pseudolymphomas

The data from the hystopathological analysis are most important for the accurate diagnosis.

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OUR EXPERIENCE WITH TOPOTECAN AS SECOND-LINE TREATMENT OF PATIENTS WITH RELAPSED SMALL CELL LUNG CANCER

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Objectives: Single agent intravenous Topotecan is an effective treatment for small cell lung cancer /SCLC/ after failure of first- line chemotherapy. The aim of this study was to evaluate the efficacy and toxicity of intravenous Topotecan in recurrent SCCC. Methods: In the period 2008-2009 seventeen consecutive patients with relapsed SCLC entered the study. The treatment schedule consists of Topotecan 1,5 mg/m2 i.v. for five consecutive days, with repetition every 21 days. Results: Overall response rate was

23,5%. Median survival was 6,4 months. Nausea, vomiting and neutropenia were most common side effects. Conclusion: Intravenous Topotecan is effective as secondline therapy for patients with relapsed SCCC with good tolerability.

Key words: Relapsed small cell lung cancer, Second- line treatment, Intravenous Topotecan, Survival

CAPECITABINE AND IRINOTECAN AS FIRST-LINE CHEMOTHERAPY FOR PATIENTS WITH METASTATIC COLORECTAL CANCER

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Objectves: Capecitabine is an oral fluoropyrimidine carbamate that is at least as effective than Fluorouracil and Leucovorin as first- line treatment for patients with metastatic colorectal cancer /CRC/. The topoisomerase I inhibitor Irinotecan has shown consistent efficacy in chemotherapy- naive patients. The aim of this study was to determine the efficacy and tolerability of Capecitabine in combination with Irinotecan /XELIRI/ as first- line therapy in patients with advanced CRC. Methods: In the period 2007-2009 twenty- one consecutive patients with metastatic CRC entered the study. The treatment schedule consists of Capecitabine 1250 mg/m2 p.o. twice daily for 14 days with a

7- day rest period and intravenous Irinotecan 180mg/m2 day 1 with repetition of courses every 21 days. Results: Overall response rate was 33,3%. Median time to progression and overall survival was 7,6 months and 15,6 months, respectively. The most common grade 3- 4 adverse events were diarrhea and neutropenia. There were no treatment-related deaths. Conclusion: These results indicate that XELIRI is a potentially feasible and clinically active regimen in patients with advanced CRC.

Key words: Metastatic colorectal cancer, First- line therapy, Capecitabine, Irinotecan, Survival

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CEREBELLAR MUTISM FOLLOWING POSTERIOR CRANIAL FOSSA SURGERY IN ADULTS- RETROSPECTIVE REVIEW OF THREE YEARS EXPERIENCE.

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The functional role of cerebellum is traditionally defined as a mere coordinator of automatic and somatic motor function. Recent studies have brought to the fore that the cerebellum also modulates neurocognitive functions. The role of cerebellum in non- motor language processing is one of the major avenues of current research. It is a paramount that neurosurgeons be aware of cerebellar mutism with regard to its occurrence in adults. The pathogenesis of this syndrome remains unclear. Controversies exist regarding whether it is a purely psychogenic disorder or an organic syndrome. The anatomical substrate also remains unknown. We believe that cerebellar mutism is a form of dysarthria rather than a psychological disturbance. Our recordings revealed that cerebellar syndrome in adults is not transient if lesions are located in the cerebellar hemispheres /6th month follow up/

. Speech disorders persist despite full recovery of other cerebellar syndromes registered before surgery and early postoperative period.

Despite the localization of the lesion-left or right hemisphere, speech disorders were revealed in all patient. Our study confirmes the theory of Broich for the "crossed cerebellocerebral diaschisis". The last one supports another one theory reported in the 1995 for the bilateral connections of cerebellar hemispheres to the Broca's area and supplementary speech area. As it's seen from our study, the vermian incision doesn't play a role in the etiology of cerebellar mutism in adults but in children it does. Further studies and reports are needed in the future to explain the pathogenesis of cerebellar mutism in adults and a supplementary treatment seems to be necessary.

A CASE OF XANTHOMA TUBEROEREPTIUM

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Xanthoma tuberoereptium is an uncommon disease in the dermatology practice. It presents deposits of different lipid fractions in the skin.

Xanthoma tuberoereptium are very small, yellow doneshaped papules, surrounded by a red ring. We present a case of xanthoma tuberoereptium in a 49 old man with symmetrically located yellow papules on the elbows and knees.

The patient showed high levels of some the lipid fractions.

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A CASE OF T-CELL PSEUDOLYMHOMA RESULTING A TREATMENT WITH D-PENICILAMIN

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D – penicilamin is a medicine that is well resorbed by gastro – intestinal tract. It is metabolized by the liver. It has the ability to connect in hilate complexes the ions of the heavy metals.

D-penicilamine is a therapeutic agent in hepato-lenficular degeneration – performed by lack of ceruloplasmin resulting in cumulation of copper in the liver and in leuticular substance of the brain.

We present a patient -69 years old male who was treated with D - penicilamine -3 times daily (3 g) for 6 months because of Wilson - Conoralov disease.

At the end of the third month the patient formed nodular redish eruption localized in retrocuricul and sub maudibular areas.

The skin biopsy showed the pattern of T-cell pseudolymhoma.

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A CASE OF PEMPHIGUS FOLIACEUS ASSOCIATED WITH THYMOMA.

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Pemphigus vulgaris is a blister disease that is characterized with appearance of blisters on normal – appearing skin and mucous membranes. It is a prototype of auto-immune disease.

Pemphigus foliaceus is a type of Pemphigus with very superficial acantholysis, producing more erosions than blisters

The course of Pemphigus foliaceus is quite chronic in adults.

Extremely rare cases may be associated with neoplastic disorders.

We present a case of Pemphigus foliaceus in a 53 years old female, who was diagnosed as Pemphigus foliaceus and in 3 months she had palpebral ptosis of right eye.

After the analysis of scanner and computer tomography the patient was diagnosed as Thymoma.

We recommend all the cases with Pemphigus foliaceus and Pemphigus vulgaris to be suspicious for neoplastic disorder.

A CASE OF ACTINIC RETICULOID ASSOCIATED WITH LUNG CANCER.

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Actinic reticuloid is a chronic cutaneous disease, connected with expressed photo sensibility to UVA, UVB as well as visible light. It could be associated with cutaneous lymphomas and with other neoplastic disorders.

We present a case of Actinic reticuloid in a 65 years old man, who had a lung cancer.

The association between these two diseases, lead to exacerbation of actinic reticuloid.

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PSEUDOLYMPHOMA CUTIS IN A SCABIOUS PATIENT

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Post scabious reaction of the skin often resembles pseudolymphoma, as in thise cases multiple thick redish pruriginous papules and nodules are seen.

They are localized – perigenitally, abdomen area, axillae and elbows. They can persist months after adequate antiscabious therapy.

Some authors propose that they are as a result of delated

type reaction of hypersensitivity towards the components of the acarus.

We present a case of pseudolymphoma in 18 years old boy. One mount after the end of the therapy we observed lymphocytoma cutis, localized on the corpus penis and scrotum, accompaned with severe pruritus.

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A CASE OF POSTTATOO PSEUDOLYMPHOMA

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A tattoo is a permanent change in skin colour, produced by introducing a pigmented particle in the skin.

Professionally the tattoos are done by sterile pigment injections specialized needles to a standard depth in the dermis. The red color is usually obtained with cinnabar (mercuric sulfide) Cobalt aluminates salts give light blue colour.

The tattoos may cause contact allergic or phototoxic

reactions, sarcoidal reaction and a microscopic picture of pseudolymphoma.

We present a 37 years old male with cutaneous pseudolymphoma placed in the red area of the tattoo. It appeared 3 mounths after the tattoo has been done.

Histological picture from the skin biopsy showed the features of B-cell cutaneous pseudolymphoma.

RAEDER PARATRIGEMINAL SYNDROME IN A PATIENT WITH A MASS LESION IN THE MAXILLARY SINUS

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Introduction: Raeder paratrigeminal syndrome is a rare syndrome, characterized by severe unilateral facial pain and headache in the distribution of the ophthalmic division of the trigeminal nerve in combination with ipsilateral oculosympathetic palsy or Horner syndrome. Raeder syndrome has been associated with several conditions, including head trauma, hypertension, vasculitis, migraine headaches, parasellar mass lesions, and internal carotid artery dissection or aneurysm.

Case Description: We describe a case of a 65-year-old male patient who presented with facial pain involving the ophthalmic and maxillar divisions of the right trigeminal nerve and ipsilateral ptosis, together with a bloody discharge from the right nostril in the last two months. Neuroophthalmological examination showed a partial Horner

syndrome (right ptosis without miosis). Basic laboratory analysis was within normal range. MRI showed a large hypointense tumor mass in the right maxillar sinus with local invasion and dissemination in the epipharyngeal lymphatic collector. The patient was sent for surgery.

Discussion: Unilateral oculosympathetic paresis and evidence of trigeminal nerve involvement are the two hallmark clinical features of the rare Raeder syndrome. While most cases are benign, a thorough evaluation and neuroimaging are necessary to exclude secondary causes, particularly if parasellar nerve involvement is evident. With the present case we would like to underline that thorough clinical examination in patients with mild ptosis is needed to ensure accurate and prompt diagnosis of possible serious underlying diseases.

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LOW DOSE INTERLEUKIN 2 IN NEOPLASMS - CLINICAL APPLICATION AND IMMUNOLOGICAL PROFILE

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Objectives: We wanted to investigate clinical efficacy of intermittent local and subcutaneous low-dose Interleukin 2 applications in patients with different malignancies not suitable for standard therapy, and to follow up changes in some immunological parameters.

Methods: Interleukin-2 was applied intratumorally, through selective hepatic artery infusion or intraperitoneally in 30 patients with different neoplasms, and subcutaneously in 17 patients. Lymphocyte subpopulations and regulatory CD4CD25high lymphocytes were analysed by flowcytometry with Simulset IMK (Beckton and Dickenson) and CD4FITC and CD25PE (BulBio NCIPD). Changes in Th1 / Th2 cytokines were measured by CBA kit (Beckton and Dickenson) and TGFb1 was measured by Elisa method (Quantikine). C-reactive protein was analysed by immunonephelometric method (Dade Behring).

Statistical analysis was performed by SPSS program.

Results: Local IL-2 application had beneficial effect in 23% (7/30) of the patients - 4 patients showed stable disease and 3 patients had reduction of ascites. Subcutaneous IL-2

regime led to stabilization of disease in 29% (5/17) of the patients. No complete or partial responses were observed. Subcutaneous regime increased blood lymphocyte count, CD8 and NK cells. No significant lymphocytes changes in blood and ascites were registered after intraperitoneal applications. Regulatory CD4CD25high cells and CRP increased after IL-2 applications. Serum IL-2, IL-5 and IL-10 levels increased after subcutaneous and intratumoral IL-2 applications. After intraperitoneal IL-2 applications only IL-2 and IL-5 increased in serum, while in ascites IL-2, IFNg, TNFa, IL-10 and IL-5 increased. Serum TGFb1 decreased after subcutaneous IL-2 cycle, while no significant changes in this cytokine were registered after local applications. Lower baseline serum levels of CRP and TGFb1 correlated with beneficial therapeutic effect.

Conclusion: Intermittent low-doses of IL-2 had beneficial effect in some patients not suitable for standard therapy. Different IL-2 regimes promoted distinct immunomodulatory effect.

ESSENTIAL TREMOR AND FRONTAL MENINGIOMA

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Objectives: Essential tremor is not frequently associated with brain tumors.

Methods: Case report

Results: We present a 74-year-old female with frontal meningioma and essential tremor. The patient has history of headache preceding the onset of postural and kinetic hand tremor, and tremor of the head and chin. After surgical tumor removal the tremor persisted and later was markedly relieved by clonazepam.

Conclusion: We discuss the potential role of frontal lesions affecting the cerebello-thalamo-cortical pathways in essential tremor.

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PARKINSONISM AND BRAIN TUMORS

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Abstract: Brain tumors rarely cause parkinsonism. They may occur in different brain regions, and may be various types: glioma, meningioma, lymphoma, fibrosarcoma, and metastases. The pathologic mechanism leading to parkinsonism is the direct infiltration of tumor cells or indirect mass effect causing impaired metabolism of the striatum.

Tumors produce their own characteristic combination of focal signs, occasionally, they can present with Parkinsonism with bradykinesia and rigidity, and rarely rest tremor

Neuroimaging is recommended for investigation of atypical parkinsonism. Brain MRI is preferred for patients with coexisting signs apart from extrapyramidal symptoms, because some mass lesions are not observed by CT scan. The symptoms of parkinsonism usually resolve completely shortly after surgery for removal of the tumor, however, residual or postoperative symptoms may persist.

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IMMUNE RESPONSE IN MALIGNANT GLIOMA

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Objective: Malignant gliomas are primary brain tumors with excessive mortality and high resistance to chemotherapy and radiotherapy. The survival time for glioblastoma multiforme is about 6-12 months. As key pathogenetic mechanisms are recognized the massive necrosis, angiogenesis and hypoxia within the tumor, as well as the resistance to apoptosis. It is also suspected that altered immune response might contribute to the fatal clinical outcome.

The aim of the present study was to determine the immune status of patients with malignant gliomas.

Material and methods:

Peripheral blood lymphocytes were collected preoperatively from 9 patients (aged 57-76) diagnosed as anaplastic astrocytoma grade III (n=4) and glioblastoma multiforme

(n=5). The following lymphocyte populations were analyzed by flow cytometry: CD19+, CD3+, CD3+CD4+, CD3+CD8+, CD3-CD56+, CD3+CD56+, CD3+CD25+, CD8-CD11b+, CD8+CD11b+, CD8+CD11b-. The results obtained were compared to reference values for each cell population. Results:

No significant alterations were detected in CD19+, CD3+, CD3+CD4+, CD3+CD8+ cells, but the CD4/CD8 ratio was below the reference range. An obvious decrease in NK and NKT cells was observed. A reproducible phenomenon of increased CD8+CD11b+ and decreased CD8+CD11b- cells was noticed.

These preliminary results suggest that the immune response in patients with malignant glioma is seriously disregulated. The rapid clinical deterioration, relapses and high mortality could be at least partially explained with the suppressed activity of NK-cells which are the major cytotoxic antitumoral cells. The increase in the population of activated suppressoreffector cells also contributes to the unfavourable outcome in malignant brain tumors.

Conclusion: This pilot study reveals the presence of altered

immune response in malignant gliomas and opens possibilities for prospective investigations concerning immune status and clinical outcome.

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ANTITHROMBIN III AND PLASMIOGEN - PROGNOSTIC INDEX OF ACUTE LIVER FAILURE

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Objectives: the present study aims to demonstrate the clinical significance of Haemostatic indices (HI) - plasminogen (PLg), antithrombin III (AT III) and prothrombin time (PT) as well as some routine biochemical tests in patients with acute viral hepatitis (ALF).

Patients: the following patients •• groups were investigated: fulminant hepatitis (FH) n - 53 and n-162 - with severe forms of acute viral hepatitis menaced of liver coma. Comparative study was performed in n - 454 patients with various forms of acute viral hepatitis.

Methods:

AT III ,Plg - coagulation and fibrinolytic methods compared to chromogenic and immunodifusion one; PT - standart method with thrombo-Plastin. Reference values: Plg activity, and PT - 80 - 120%; AT III - 44 B•" 175% activity.

Results:

Plg activity was found to be reduced in AVH in accordance to the severity of the liver damage. AT III activity was increased or normal in severe forms of AVH, and reduced in patient menaced of liver coma. With Plg below 20% in combination with reduced AT III activity were menaced of aggravation and liver coma. Of total number of parallel investigated PT and Plg - 85% of the PT test are in normal range versus 15% for Plg. Ot 186 normal PT test, only 33 (18%) are in association with normal Plg test; Plg tests are in the interval groups of 60 - 80%; 62 (33%) - in interval of 40-60%; 59 -41%) between 20-40%; and 3 (2%) - between 10-19%. Mean SD by FH was 42+/- 26% for PT versus 13+/-11% for Plg. It is noteworthy that the dynamic in the level of haemostatic indices - Plg and AT III preceded the clinical symptoms of aggravation or improvement with 2 - 7 days in AVH and with more than 30 days in progredient or chronic hepatitis.

Conclusion: Plg and AT III are more sensitive liver functions tests as prognostic indices of AVH and Fulminant hepatitis than PT.

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ACERBINE UNGUENTUM IN THE LOCAL TREATMENT OF PALMOPLANTAR PSORIASIS

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Acerbine unguentum combines malic, salicylic and benzoic acids in the standard formula, that provides regular distribution above the affected area and supports the healing process. The medication is well known for years in therapeutic practice for the treatment of stasis ulcers, surface burns and cut wounds.

Psoriasis palmoplantaris is broadly widespread condition, characterized by dryness and multiple painful fissures on the palms and soles, situated on a hyperkeratotic base. Objectives:

To assess and discuss clinical effectiveness of Acerbine

unguentum in treatment of fissures in patiens with palmoplantar psoriasis.

Methods:

Acerbine unguentum was administered locally in the area of fissures for a 21 days period in 26 outpatient and inpatient cases with histology proven psoriasis palmoplantaris.

Results and conclusion:

We observed a very favourable effect, epitelisation and reducing the pain in affected limbs in all patients whiteout any secondary complications.

STUDY OF THE NORMAL ULTRASTRUCTURE OF THE MESENCEPHALIC TRIGEMINAL NUCLEUS OF THE HUMAN

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Studies of sensory nuclei of trigeminal nerve and especially of mesencephalic trigeminal nucleus (MTN), dates from 1896. RamFin Cajal in experimental animals observed in the first embryonic cells (MTN). Neurons observed by him have small, short and branched dendrites. It was found that during the development of the organism ontogenetically they are absorbed. Subsequently, the characteristic shape of the nucleus pseudounipolar neurons. Golgi method using impregnation, seen this type of cells described in rodents.

Although the core research lasting more than a century and today, the interest of neuromorphologists in this structure arouses interest and give rise to different boards. Over the last decade have been conducted numerous anatomphysiology studies Lazarov (2005) on neurons located in (MTN) in different experimental animals. In this work we present a normal C•ytoarchyteconic (MTN) in man using electron microscopic research.

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NEUROCHEMICAL AND COMPARATIVE CHARACTERISTICS OF MESENCEPHALIC TRIGEMINAL NUCLEUS IN HUMANS AND CAT

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In 1846 Stilling, describing the nuclei of Cranial nerves located in the middle of the brain and special n. trochlearis brainstem differs in three parts in this nerve. The author assumes that the lower part of the nucleus of nerve,\'\'pars inferior nervi trochlearis\'\'is the place from which mesencephalius root is separated of n. trigeminus. Deiters (1865), observing neurons located around the cerebral aqueduct, founds that they are similar to cells of the trigeminal ganglion. He takes the view that these neurons,

regardless of their proximity placement with nerve trochlearis probably belong to the sensory part of n. trigeminus. The first, which clearly distinguished cluster of neurons along the middle brain in an independent core is (Meunert 1871). Before his research mesencephal nucleus of trigeminal nerve is attributed to trochlearis nerve. We present neurons located in the mesencephalic trigeminal nucleus per person and compare their morphological characteristics with neurons in experimental animal cat.

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CYTOARCHITEUTONICS OF MESENCEPHALIC TRIGEMINAL NUCLEUS IN MAN

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Johnston (1909) describes the mesencephalic trigeminal nucleus (MTN), located in the root as the brain substance of the average level of the brain and descending along the outer side of the head (trabesto) gray matter of the cerebral aqueduct. MTN passes through the rostral part of the bridge, increasing their volume and constant number of

those in neurons and it is exhausted to the floor of the fourth ventricle. Successive histological preparations it is presented as a strand in the shape of a crescent. We present a cytoarchitetonic MTN with lightmicroscopic methods. For this purpose, we have used Nissl staining.

MESENCEPHALIC TRIGEMINAL NUCLEUS-SPUTUM CYTOLOGY COUNTS

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Form of mesencephalic trigeminal nucleus (MTN) and the external morphology of its neurons are extensively studied using classic staining techniques and light microscopy. At RamΓin Cajal (1909) describes two parts of (MTN) in experimental animals: upper or lower tail and head or part of the kernel. The first consists of scattered cells, while the second is more compact and is made up of larger sized cells. Morphological studies of Willems (1911) and physiological experiments Jerge (1963) subsequently proved that (MTN),

similar to the motor and distinction from other sensory trigeminal nuclei, there somatotopic differentiation. Because of the dual embryonic origin (MTN) - combo of nerve and pinnate plate could be expected non-hommogen cell composition. We present a heterogeneous structure (MTN) of lightmicroscopia with different magnifications. A small increase highlighted the form of (MTN) in man, arranged as columns along Middle cord and terminating in the rostral part of the bridge, where it significantly expands its volume.

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GRAPHICAL REPRESENTATION OF NEURONS LOCATED IN TRIGEMINAL GANGLION IN HUMANS AND EXPERIMENTAL ANIMALS.

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In the studies we decided to do measuring the size of neurons and their density, as in man and in cat and comparable data received. Morphometric analysis was performed using a computerized system for analyzing images of Olympus. Neurons were measured in preparations of human and cat and the results were presented in tables and charts. Neurons separated according to size of their diameter into three main types: large, medium and small. After determining the area of neurons in the human and the cat had compared them.

According to the perikaryon shape and intensity of color, according Nissl accumulation of granular neurons of the typical split (oval light and dark oval) and with other atypical form of pseudounipolar neurons (light and dark). The calculated density of neurons, the number of 1 mm2, is presented in tables and graphs. From the analysis of statistical data can be concluded that the density of neurons in the cat is much higher than that in humans, but its neurons, regardless of which type they belong, have larger dimensions /areas/.

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PRESENTATION OF THE LIG.SUSPENSORIUM DUODENI IN HUMAN

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The end of the ligament is projected between designing tr coeliacus and freely displayed initial part of the trunk of a.et v. mesenterica sup. or is it the middle of the line between tr coeliacus and the intersection of the upper edge of the horizontal part of duodenum is available as a left approximately one cm. from the line that connects a and tr coeliacus. mesenterica sup. In depth this end projects over the left diaphragmatic varhuu feet. On skeleton it is

disposed on the level of intervertebrae the height of the disc at Th12 and L1. We present using histological methods the morphological structure of ligaments. After standard processing for light microscopy colors used in Nissl. For the current study we have used human material accumulated. Histological sections were taken at the described level. The prepared histological preparations were observed under various magnifications.

LIGHT-MICROSCOPIC STRUCTURE OF LIG. SUSPENSORIUM DUODENI

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Treyche ligament is essential for morphological and clinical subjects, which unfortunately is poorly addressed in the literature. Anatomical part of it is presented as part of strengthening and fixing apparatus of the duodenum. It also participates in maintaining the body of the pancreas in a horizontal position. Because of its topographical relationship to the rear abdominal wall, tr coeliacus,

duodenum and pancreas, it is of interest, both morphologically and clinically. For the current study was used human accumulated material taken during surgical interventions on the occasion of presence of Ca in the stomach. The material was processed by standard technology for light microscopy. We have used various coloring techniques.

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NUCLEI PERIAQUEDUCTI GREY - STRUCTURE

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Nuclei periaqeducti grei (PAG) is a tight cluster of neurons located near the aqueduct along the middle brain. In transverse cross-section of the brainstem at the level of coliculus bodies in middle brain in human, even macroscopically clearly can be distinguished gray substance. The literature reference found in the last decade, shows that this structure is still valid because it's influence on stress. Stress reactions occur under the influence of

different mechanisms associated with activation of multiple systems in the body. Therefore a thorough study of the morphological characteristics of neurons located in this structure is particularly relevant to the present morphology (PAG) with lightmicroscopic methods. To visualize the neurons we have used standard method for staining of Nissl.

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SOME PSYCHOPATHOLOGICAL PECULIARITIES OF EARLY AND LATE ONSET ALZHEIMER'S DISEASE

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The aim of our work was to explore the manifestation of some psychic (non-psychotic and psychotic) and behavioral symptoms of patients with early onset (EO-AD) and late onset (LO-AD) of Alzheimer's disease (AD) with a view to compare and enrich the clinical, diagnostic and differential diagnostic possibilities.

Objectives: 38 EO-AD and 72 LO-AD, hospitalized for the first time at gerontopsychiatry department of MHAT "St. Marina" - Varna.

Methods: Clinical examination, MMSE, and Neuropsychiatric Inventory (NP)/ were used. Patients were diagnosed according to ICD-10, DSM-IV Pë NINCDS/ADRD criteria for probable AD. Patients were with mild, moderate and severe dementia.

Results: Anxiety, paranoid delusions, major depression and paranoid-hallucinatory syndrome, singly or on a syndrome level, were most frequent in the two groups. Apathy,

physically and verbally non-aggressive behaviors were the most often behavioral symptoms met.

The clinical picture of EO-AD was richer of psychotic symptoms, compared to LO-AD. We found out a tendency of greater frequency of delusions of reference, harm, persecution, poisoning and relatively more frequent visual hallucinations in EO-AD, while anxiety was significantly greater in LO-AD. The comparison on a syndrome level revealed significantly more frequency of paranoid and paranoid B* "hallucinatory syndromes in moderate dementia and EO-AD, than in LO-AD. Depression in EO-AD and mild dementia had a tendency to prevail over depression in LO-AD and mild dementia, while in anxiety the relations were opposite.

As a whole, behavioural disorders were more frequent in EO-AD than in LO-AD patients. Physically non-aggressive, verbally aggressive and physically aggressive behaviors

were more often met in EO-AD patients.

As a conclusion, we suggest, that these data could represent clinical support of dividing AD not only according to the age of onset. We would like to emphasize, that the number of examined patients was comparatively small. That is why we comment some of the data as a tendency.

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DEPRESSIVE DISORDERS IN EPILEPSY

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Depression is the most frequent psychiatric comorbidity in epilepsy but very often remains unrecognized and untreated. The reported rates of depression range from 8-48%/mean 29%, median 32%/.

Objectives: We examined 103 epileptic patients, aged 18-60 years, 40 males and 63 females, for the presence of interictal depression.

Methods: All subjects underwent clinical psychiatric examination, including evaluation on Hamilton Depression Rating Scale /HAM-D-17/. A specially designed questionnaire for demographic and seizure-related variables was also completed.

Results: Concurrent depression /clinically presented and according to ICD- 10 diagnostic criteria/ affected 29% of all evaluated patients. Based on HAM-D-17 scores depression was categorized as mild- 80% of all depressed patients, moderate- 17% and severe- 3%. Among all depressed patients 60% had partial seizures, accompanied or not by secondary generalization /according to ILAE classification/ and 40% had primarily generalized seizures. Seizure free were 10% of all depressed subjects, 23% had less than one seizure/month and 67% had seizure frequency >1/month. Atypical presentation of interictal depression was frequent.

A pleomorphic cluster of symptoms of depression with a chronic course and intensity characterized by fewer neurotic traits, higher trait and state of anxiety, especially related to seizures, high irritability, explosive anger and somatic symptoms as pain especially headache, disturbed sleep, decreased energy, tiredness and fatigue were observed. Overestimated ideas of worthlessness and guilt reported 37%, suicidal ideation 10% of all depressed patients. Impaired concentration or ability to think was registered too. Risk factors for depression included: neuroepilepsy, psychosocial variables, antiepileptic medication and sociodemographic factors.

Conclusion: Depression has a tremendous effect on one's family, social and psychological functioning, even more than the actual seizure frequency and severity. Diagnostic difficulties come through the atypical mode of presentation of depression in epilepsy to which many authors refer as dysthymic-like disorder of epilepsy. Given the chronicity of the disorder many patients and specialists assume that it is a part of the epilepsy itself and underestimate pharmacologic treatment options. Proper neuropsychiatric evaluation is essential for improving treatment and quality of life for patients with epilepsy.

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ACUTE INTOXICATIONS WITH BENZODIAZEPINES

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The acute intoxications with benzodiazepines take main place among the medicamentous intoxications. A retrospective analysis of acute intoxications with benzodiazepines in Varna region for a 15-years period (1991-2005) has been performed. It was established that they were the cause of hospitalization of 1350 patients (10,74%) of the total number 12565 patients, treated for acute intoxications in the Toxicology department for the same period. The acute intoxications with benzodiazepines are 26,9% of all medicamentous poisonings. 1038 (76,89%) are female and 312

(23,11%) are male. These poisonings were significantly more frequent in female population. The ratio between female and male patients is 3,32:1. In most cases these poisonings were in the age group up to 24 years - 734 patients (54,37%). Only 56 patients (4,15%) were ower 60 years old. The main reason for these poisonings are the suicidal attempts - 1259 patients (93,26%). The intoxications with benzodiazepines are cause of death for 3,03% of all acute poisonings. A consistent trend of reducing the incidente of benzodiazepines intoxications is established in the end of the period.

A NEW MANAGE IN THE TREATMENT OF CHRONIC URTICARIA WITH DESLORATADINE

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Chronic urticaria is urticaria persisting more than 6 weeks. This form is quite difficult for treatment.

Most of the dermatologist use steroids, antihistamines or both with doubt effect.

One of the contemporary antihistamines is Desloratadine 5 mg.

We treated 20 patients (13 females and 7 males) with 4 tablets (2 tablets in the morning and 2 tablets in the evening) before meals for 30 days.

No adverse events or sedative reactions were observed. This treatment scheme is excellent for chronic urticaria, avoiding the use of steroids.

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A CASE OF PRURIGO NODULARIS ASSOCIATED WITH DIABETES MELLITUS

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Prurigo nodularis is a very pruritic dermatosis, characterized by persistent nodules. It considers as pathognomonic for uremia; renal disorders.

The biggest group of patients with prurigo nodularis has atopic dermatitis or at least an atopic diathesis. Another group of patients has a emotional risk, such as depression and psychosocial problems.

We present a case of prurigo nodularis in 54 years old female.

She developed the disease 3 years ago with presence of nodular pruritic lesions to the distal aspects of the extremities

Blood analysis showed elevated serum IgE and high levels of blood sugar.

Prurigo nodularis is a rare dermatose that could be associated with endocrinic disorders – diabetes mellitus as well as already known

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THERAPEUTIC SCHEME FOR TREATMENT OF ROSACEA WITH AZITROMYCIN.

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Rosacea is a common disease more often in women and not so often in men. Clinically it involves the mid-face in which papules and pustules develope on a congestive erythematous teleangiectatic background.

They may cause sebaceous gland hyperplasia and fibrosis and developing rhinophyma.

The treatment of rosacea is quite difficult, especially when it depends on hormonal and actinic factors.

We present a scheme for treatment with azitromycin.

The treated group is 17 females and 8 males, average age 30-60 year for males and females.

All of them took azitromycin – 500 mg. daily for 1 week and 7 weeks – 250 mg – 3 times per week. All of them used photoprotection.

Very good results were observed at the end of the treatment, as well as 1 and 2 months afterwords.

TREATMENT OF PLANE WARTS WITH IMIQUIMOD 5% CREAM

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Plane warts are firstly described by Besnier and Doyon in 1881 d.c. They are small flat papules often slightly hyperpigmented and most commonly found in the face. They are typically seen in children and young adults. They may also occur on the hands, arms, trunk and beard.

A wide range of a therapeutic measures is available but no one regimen is highly effective.

Imiquimod is an immune response modifier. Clinical studies have demonstrated induction of cytokines, including alpha interferon, following application of imiquimod.

15 patients (12 females and 3 males) who had plane warts were treated with imiquimod (Aldara 5% cream) for 8 weeks. The cream was applied three times per week prior to sleep. The cream leaved for 6 to 10 hours.

All the patients had light irritation at the beginning of the treatment including erythema, erosion, excoriation, flaking and edema.

All the signs resolved within 1-2 weeks of discontinuation.

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CAUSES OF DEATH OF THE ACUTE INTOXICATIONS

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The death rate of the acute intoxications in the clinic of toxicology in Varna for the period between 1991-2009 was analyzed. The study included 16603 cases and 197 of them were lethal autcome. The death rate is 1,19%. 126 (63,96%)of them were male and 71 (36,04%) were female. The connection between the progress of the age and the increase of the lethality is established. The main cause of the death of

acute poisoning are: alcohol- 55 cases (27,92%), pesticides - 51 cases (25,89%), medicines - 43 cases (21,83%), Amanita phalloides poisonings - 25 cases (12,69%). Reasons for the rest 23 lethal cases are intoxications with corrosive substances, opioid poisonings, inhalatory toxic substances, acute toxoallergic reactions.

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ETHANOL ABSTINENCE-APPARENT AND POTENTIAL PROBLEMS.

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Ethyl alcohol is the most common abused chemical substance nowadays. The real frequency of ethanol dependency is underestimated as many patients do not realize it and do not seek medical help. The authors observe 176 patients with toxic ethanol effects treated at the department of Toxicology during 2007 year. 64 (36.36 %) of them had ethanol abstinence. 59 (92.18 %) were in active age-between 20 and 60 years. The cause of withdrawal was cessation of drinking or a reduction in intake because of illness, surgical operation, isolation, lack of money. 20 patients (31.25 %) did not realize they were alcohol dependent. Toxic chemical analysis showed no ethanol in the blood in 57.78 %; 0.1-0.5 in 11.2 %; 0.5-1.0 in 4.44 %; 1.0-2.0 in 8.88 %; over 2 -in 17.7 %. All the patients had typical alcohol abstinence syndrome with moderate or

severe expression. All of them had toxic ethanol hepatitis. The following complications had been observed: seizures, long lasting severe delirium, severe mono- and polyneuropathy, myelosuppression, pneumonia, pancreatitis, cardiac failure. All the patients were consulted by a psychiatrist. In 16 cases a co-existing psychiatric disorder was established. The duration of the hospital treatment was between 2 days and 26 days.

Some potential problems connected with alcohol abstinent patients in case of mass disaster are disscussed. Abstinent patients, especially when inadequate, could break the quarantine and other restrictive rules, have antisocial and criminal behavior, increase the panic etc. They also can be more sensitive to toxic chemical agents attacking the CNS or liver. As ethanol abstinence is a serious medical condition

it requires an urgent specialized medical help and engages many specialists and medical teams.

The authors suggest that a more thorough preventive investigation and treatment of the existing alcohol

dependence would reduce the frequency of severe abstinent states.

Key words: ethanol, abstinence, delirium, complication, toxic chemical analysis.

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TOXIC LIVER DAMAGE CAUSED BY NARCOTICS AND ANABOLIC STEROIDS

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We present two clinical cases of narcotic and anabolic steroid liver damage. The first one was a patient with a light toxic liver damage after regular misuse of steroids, anabols, cocaine and amphetamines. The second one was 17-years old patient with a fatal liver failure after regular misuse of alcohol and anabols.

The mechanisms of liver damage development are disscussed: receptor or non-receptor interaction; as a result of the metabolism of narcotic substances and covalent binding to cell structural proteins; active radicals;

autoimmune processes. The authors submit for disscussion data about hepatal toxicity of some of the most common abused narcotic substances like ecstazy (3,4-methylenedioxy-methamphetamine), amphetamines, cocaine, "angel dust" (phenylcyclidine), marijuana (THC), psychoactive mushrooms, LSD (lysergicacid diethylamide), heroine, anabolic steroids.

Key words: liver damage, anabolic steroids. ecstazy, amphetamines, cocaine, phenylcyclidine, marijuana, psychoactive mushrooms, LSD, heroine.

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PROGNOSIS FOR DISASTERS CAUSED BY ACCIDENTS IN THE REGION OF VARNA BULGARIA

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Medical University of Varna, "Prof. P. Stoyanov"

Disastrous situations result from the action of natural and technological (anthropogenic) factors. The technological disasters become more common due to the considerable progress in the field of modern industrial technologies. They represent a permanently threatening potential danger for the world as a whole, for Bulgaria and for the region of Varna as well. The production capacities and the stored and used industrial toxic substances along with the natural-

geographic peculiarities contributing to the polluted territory after accidents in the region of Varna were analyzed. A flexible and rapidly adapting organization of medical service in case of disasters was created.

Key words: Disaster; Industrial toxic substances; Environmental factors; Medical service in disasters; Region of Varna

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MEIGE SYNDROME. REPORT OF TWO CASES.

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Objectives: Meige syndrome, first described in 1910 by the French neurologist Henry Meige, is a rare condition characterized by oromandibular dystonia and blepharospasm.

Methods: Case reports

Results: We report 2 cases of Meige syndrome. Patient 1, a

34-year-old female, presented with complaints of frequent eye blinking which had appeared 4 months earlier, after emotional distress. She reported episodes of forceful complete closure of the eyes, jaw contraction, and involuntary mouth movements. The involuntary movements were disappeared during sleep, relieved after sleep, and in

some occasions the patient succeeded in suppressing them. At the neurology department she presented with symmetric bilateral blepharospasm, involuntary dystonic movements of jaws, lips and tongue. Patient 2, a 68-year-old female, complained of involuntary eye blinks which had become more frequent lately, followed by unwilling masticatory movements, dating back from 3 years. During this 3 year period she was not consulted by a neurologist. Her neurological examination revealed bilateral blepharospasm and forceful contractions of the jaws.

Conclusion: We discuss the occurrence of some cases of Meige syndrome in association with or secondary to another disorder such as tardive dyskinesia, Wilson disease, and Parkinson disease. Other conditions to be considered are tardive dystonia, hemifacial spasm, benign essential blepharospasm, temporomandibular joint dysfunction. Coexistence with myasthenia gravis is described that could lead to diagnostic confusion and delay appropriate treatment.

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DECIMETER WAVE THERAPY IN LATE PARKINSON'S DISEASE

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Objectives: Late stage Parkinson's disease (PD) is characterized by significant worsening of symptoms, motor fluctuations and decrease of effectiveness of drug therapy. Decimeter wave therapy (DWT) is an option to expand treatment strategy in late PD.

Methods: We studied the effect of DWT in 7 patients (4 males), aged 67,72 years, with 7,14 years of disease duration. Four were at Hoehn- Yahr stage III and the remaining 3 were at stage IV. Mean UPDRS total score sum was 39,86, and mean UPDRS part III sum was 24,86. DWT was performed according to a standard protocol using a "Volna- 2" apparatus, 10 consecutive procedures, once daily. Evaluation of UPDRS total and part III was performed on baseline, on days 11, 31 and 61.

Results: On day 11 all patients showed decrease in both UPDRS total and part III. We lowered the levodopa doses of 3 patients in Hoehn- Yahr stage III with greatest decrease of UPDRS. On days 31 and 61 UPDRS total and part III were still lower.

Conclusion: Our results demonstrate the substantial effect of DWT on motor symptoms in late PD patients. All patients showed improvement, demonstrated by UPDRS, as the effect still lasted for 2 months after the physical therapy, though slightly diminished on day 61, compared to day 11. According to our results and patients' subjective satisfaction reported, we could propose DWT to become a part of the treatment strategy in late PD patients.

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CLINICAL CRITERIA FOR PROGNOSIS OF THE DURATION OF HOSPITAL TREATMENT IN CASES OF ACUTE INTOXICATIONS WITH ORGANOPHOSPHATES

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Several criteria have been suggested to estimate the intoxication severity, yet so far no system of clinical criteria has been developed to determine the duration of hospitalization. The forecast is linked to the influence of the extended corrected QT interval and GCS (Glasgow Coma Scale) on the frequency of the developing acute pulmonary insufficiency and lethality. The average duration of hospital treatment is also crucial. First of all it is determined by the intoxication severity and lasts from 3 to 26 days. The aim of this study is to develop an individual forecast about the duration of hospitalization for patients suffering from acute exogenous intoxication with organophosphorus pesticides.

The subjects are 160 patients. We use statistical regression analysis to study the significance of 5 of the most typical clinical indicators of organophosphorus intoxication on the duration of hospitalization: type of conscience, presence of spasms, pulmonary edema, shock and multi-organ insufficiency syndrome (MOIS). To forecast the treatment length we obtain simplified mathematical expressions in the form of score estimates. We confirm the significance of the clinical indicators "MOIS", "conscience" and "spasm". We build a forecast matrix that gives the opportunity to forecast the personal duration of hospital treatment for each patient.

CLINICAL CRITERIA FOR THE FUTCOME FORECAST OF ACUTE EXOGENOUS INTOXICATIONS WITH ORGANOPHSPHORUS PESTICIDES

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The wide-spread use of organophosphorus pesticides (OPP) and their substantial toxicity determine the high frequency of poisoning with them. Despite the modern treatment methods, the acute exogenous intoxications (AEI) continue to exhibit high lethality and are the source of one of the most serious problems in the clinical toxicology. A number of not commonly accepted criteria have been suggested to estimate the gravity of the organophosphorous intoxication. Until now no system of clinical criteria exists that would forecast the outcome of this type of acute poisoning. The aim of this study is to develop an outcome forecast of AEI

with OPP with the help of basic clinical criteria. The subjects of the study are 160 patients. We explore the significance of five of the most typical clinical indicators of the acute poisoning with OPP for the outcome of the intoxication and the need of artificial pulmonary ventilation, with the aid of discriminatory statistical analysis. The selected indicators form a discriminatory model with automatically built discrimination function. The obtained classification coefficients allow us to construct a forecast matrix containing score estimates designed for practical applications.

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ORGANOCHLORINE PESTICIDES AND POLYCHLORINATED BIPHENYLS IN BLACK MUSSELAND GOBY FROM BLACK SEA, BULGARIA

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Objectives: Polychlorinated biphenyls (PCBs) and organochlorine pesticides (OCPs) are nonpolar, highly lipophyllic and ubiquitous environmental pollutants. Both are classified as Persistent Organic Pollutants (POPs) and are present in the contamination pattern of marine environments world-wide. Dietary intake, especially of marine organisms, is considered the most important source of organochlorines in humans. Even at lower concentration the pesticides ease the human immune system, while higher concentration of POPs have possible mutagenic and carcinogenic effects of humans.

Concentrations of persistent organic pollutants including polychlorinated biphenyls (PCBs) and organochlorine pesticides (OCPs) were measured in two marine species: black mussel (Mytilus galloprovincialis lam) and goby (Neogobius cephalarges). Samples were collected from Lake Varna and Varna Bay in the period of 2004 - 2005 in order to evaluate the status, spatial distribution and potential sources of pollution in these areas. The mussel, one of the most widely used bioindicators of persistent organic pollutants, has been used to monitor PCBs and DDTs contamination trends in Lake Varna and Varna Bay. Black sea gobies are non-migratory species and feed mainly with benthic organisms.

Methods: The samples were immediately frozen (-18oC) after sampling. In the laboratory, the edible tissues of fish and mussels were homogenized and sub-samples of 10 g were

taken from it for extraction. The OCPs were extracted with hexane/ methylenchloride (3/1 v,v) in Soxhlet apparatus, the extracts were evaporated to allow the determination of lipid content and purified by column chromatography. The OCPs were determined by capillary gas chromatography with electron-capture detector or mass spectrometry allows better identification of OCPs. Pheasured OCPs are: Total DDTs as sum of pp-DDT, pp-DDD and pp-DDE and Total PCBs as sum of 14 PCB congeners (28, 31, 52, 77, 101, 105, 118, 126, 128, 138, 153, 156, 169, 180).

Results: Concentrations in black mussels ranged from 6.3 to 13.2 ng/g fresh weight for total DDTs. The mussel samples taken from Lake Varna showed that the results regarding DDTs contamination are higher than those from Varna Bay. Total DDTs concentration in goby ranged from 17.5 to 70.0 ng/g fresh weight. The concentration of DDTs in goby collected from Lake Varna was lower than the DDT's concentration in goby from Varna Bay. DDTs were the predominant organohalogenated contaminants in all species, with the p,p- DDE contributing to more than 70% to the total DDTs. The analysis of goby during the study period 2004 - 2005 showed a mean total load of DDT pollutants 47.6 ng/g fresh weight.

Total PCB concentrations in goby varied in the range of 0.4 and 24.0 mg/kg product. Our results indicate that PCBs contamination of goby from the Lake Varna is lower compared to the results from Varna Bay. In mussels total

PCB concentrations from the Varna Bay (0.0003 mg/kg product) were lower than those from the Lake Varna (17.5 mg/kg product).

Conclusion: The levels of OCPs and PCBs in black mussels and goby from the Lake Varna and Varna Bay were comparable with those found in other parts of the Black Sea coast. Human health risk assessment was undertaken to evaluate potential risks associated with the consumption of the varies marine species. The experimental data present initial investigations from a profound study of PCBs and DDTs in fish and seafood from Black Sea.

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ALCOHOLABUSE ENHANCES SYSTEMIC INFLAMMATORY RESPONSE IN PATIENTS AFTER SPONTANEOUS INTRACEREBRAL HAEMORRHAGE

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OBJECTIVE: To investigate the role of inflammation in the complex pathophysiology of spontaneous intracerebral hemorrhage (sICH) by assessing the relationship between serum C-reactive protein (CRP) levels and some clinical and neuroradiological parameters. The aim of the study was also to search for potential additive effects of the modifiable vascular risk factors on the serum levels of CRP.

PATIENTS: We studied 46 patients with sICH, who were admitted at the Department of Neurology and Neurosurgery, University Hospital - Pleven, Bulgaria. Serum CRP levels were measured within the first 48 hours of the disease onset and analyzed in relation to neurological deficit severity and clinical outcome after sICH. A detailed analysis of the impact of vascular risk factors on the inflammatory marker levels was performed.

RESULTS: We found enhanced CRP levels in patients with severe neurological deficit as assessed by the National

Institutes of Health Stroke Scale (NIHSS) score. Significantly higher CRP levels were found in patients with progressive clinical deterioration and worse outcome, as well. Furthermore, the serum CRP levels were higher in patients with a history of alcohol abuse.

CONCLUSIONS: Our results point out inflammation as a crucial factor in the brain injury following sICH. They suggest that a nonspecific inflammatory marker like CRP may serve as an additional diagnostic and prognostic test indicator in the acute stage of sICH. Thus, providing an opportunity for therapeutic interventions while the patient is still at the clinic. Patients with history of systemic alcohol abuse demonstrate stronger inflammatory response, an indicator for worse prognosis.

Key words: Intracerebral hemorrhage, inflammation, CRP, alcohol abuse, arterial hypertension.

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COMPARISON BETWEEN THREE LABORATORY MARKERS - LEUCOCYTE'S COUNT, CRP AND IL-6 BLOOD CONCENTRATION IN INTRAAMNIOTIC INFECTION DIAGNOSTICS.

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Intraamniotic infection is one of the common causes of preterm birth (PTB). In most cases, the infection has subclinical manifestatation and only laboratory markers can be used for its detection. The aim of our study was to compare the diagnostic capability of the blood markers: Leu count, CRP and IL-6 in the detection of intraamniotic infection in PTB. The measured average values of the three markers differ significantly in the preterm group compare to the control (full term) group. By the upper limits of the norm of the markers, the following incidence rates of infection were determined: increased Leu – 26.7% in the PTB group and 3% in the term group, increased CRP – 51.7% in the

PTB group and no evidence of infection in the control group; IL-6 over 11 pg/ml – 66.7% in the PTB group vs. 16.7% in the full term group. The infection was diagnosed with CRP and IL-6 at least 12 hours prior to increasing Leu count. The investigated markers have the following sensitivity, specificity and accuracy in detection of intraamniotic infection (confirmed histologically): for Leu – 93.3%, 25% and 47.8%, respectively, for CRP - 100%, 53.4% and 69.3% and for IL-6 - 90%, 70% and 76.7%, respectively. From the obtained results a conclusion can be done that IL-6 has the best diagnostic profile, followed by CRP and leucocytosis

DISSECTION OF CAROTID ARTERY - CASE REPORT

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Objective: The term dissection refers primarily to an elevation or separation of the intimal lining of an artery from the subjacent media and, less frequently, to separation of the media from the adventitia. Dissection is usually accompanied by hemorrhage into the arterial wall. According to the literature serious vascular injurie to the neck may be asymptomatic or masked by other life-threatening conditions.

Material and methods: We observed one patient - 44 years old men/, with multiple trauma to the neck and left leg, three months before the hospitalization, suffering from acute ischemic stroke. There were no risk factors for cerebrovascular disease. CT angiography was obtained by Spiral Scanner with reconstructions and interpretation by a radiologist. Color-coded duplex sonography was used to

determine the extracranial blood flow velocity and the wall of carotid arteries.

Results: Angiographic examination revealed a dissection of left common (distal part) and left internal carotid artery (proximal part) - 6.5 cm long. Considerably higher peak systolic velocity (PCV) and asymmetry PSV left/right ratio of common carotid artery was found.

Conclusion: According to our study CT angiography of the carotid arteries and color-coded duplex sonography in cervical trauma may be used as an accurate decisive tools for a needed surgical intervention. More studies with larger number of patients and comparison with angiography and sonography are needed.

Key words: dissection, carotid artery, CT angiography, color-coded duplex sonography

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CORRELATIVE NEUROSONOGRAPHIC AND NEUROIMAGING STUDIES IN ASYMPTOMATIC ISCHAEMIC DISTURBANCES OF THE CEREBRAL CIRCULATION AND ARTERIAL HYPERTENSION

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Objective: To evaluate the correlation between the arterial hypertension and changes of carotid arteries and cerebral parenchima in patients with asymptomatic ischaemic disturbances of cerebral circulation (AIDSS) using comparative neurosonographic and neuroimaging studies. Material and Methods: The study included 93 patients with AIDCC, 30 patients with risk factors (RF) for cerebrovascular disease (CVD) and 78 healthy subjects . The patients were devided in two groups depending of the stage of arterial hypertension (AH): stage I [140-159/90-99], stage II AH [160-179/100-109], stage III AH [e"180/e"110]. Colour-coded duplex sonography was used to determine the extracranial blood flow velocity and the intima media thickness (IMT) of common carotid arteries (CCA), the presence of atherosclerotic plaques, their severity, echogenicy and stability. A paralell magnetic resonance imaging (MRI) was applied.

Results: Healthy persons were without RF for CVD and had normal sonographic and MRI parameters. In AIDCC the changes in carotid blood flow and cerebral parenchyma progressed with the increase in duration, severity and nonsystemic treatment of AH. There is a negative correlation between duration of AH and cerebral blood flow velocity in AIDCC. Compared to controls and patients with RF for CVD in the group with AIDCC enlargement of the ventricles and trend to confluens of white matter lesions in patients AH stage III was found.

Conclusion: This study confirms the leading role of duration, severity and type of treatment of AH in the pathogenesis of AIDCC.

Key words: AIDSS, arterial hypertension, neurosonography, neuroimaging

UNILATERAL PROPTOSIS: A DIAGNOSTIC CLINICAL AND NEUROIMAGING CHALLENGE

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Introduction: The differential diagnosis of unilateral proptosis includes tumors, infections often related with immunological process, trauma, vascular diseases or axial myopia. This heterogeneous group of conditions needs multidisciplinary diagnosis and management. Accordingly, we report two cases with unilateral proptosis.

Case I: A 34 year old male with a 3-months history of proptosis of the left eye with diplopia and normal visual acuity was admitted to our clinic. Initial CT scan examination showed highly suggestive finding for orbital apex tumor or glioma of the optic nerve. Because of normal visual acuity and normal fundoscopy a second CT scan with complementary projections was performed. A highly swollen inferior rectus muscle that simulated an orbital apex tumor was visible. A diagnosis of unilateral thyroid ophtalmopathy was made.

Case II: A 56 year old female with unilateral exophthalmus

and medical history of Graves' hyperthyroidism was hospitalised in our clinic. Previously Graves' ophthalmopathy was suggested. Neuroophthalmological examination showed hyperglobus of the right eye-exophthalm 5 mm greater on the right side. Snellen visual acuity was normal for the left eye (6/6) and 6/6 with - 7.0 dsph for the right eye. Fundoscopy showed myopic fundus. The CT scan revealed normal extraocular muscles without swollen. A diagnosis axial myopia was made.

Conclusion: These two cases of unilateral proptosis are reported because of their clinical and radiological differential diagnosis. Their description suggests that the accurate recognition of a unilateral proptosis remains a big challenge for the clinicians.

Key words: unilateral proptosis, orbital apex tumor, optic nerve glioma, differential diagnosis

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COMPARISSON OF FDG-PET, MORPHOLOGICAL NEUROIMAGING AND EEG FINDINGS IN EPILEPSY

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Background: Epilepsy is one of the most common neurologic disorders and affects approximately 1% of the population. Although, EEG is accepted as a gold standard and MRI demonstrates morphologic changes in approximately 80% of patients, the structural lesions may not always correlate with clinical, EEG and pathologic localization of the epileptogenic foci. Interictal PET as a non-invasive focus-localizing technique measures regional glucose metabolism with sensitivity up to 85%.

Objective: To evaluate the usefulness of interictal (18) F-fluorodeoxyglucose (FDG) PET/CT for detecting epileptic foci compared to the EEG and structural neuroimaging findings.

Material and methods: A total of 18 patients (7 males and 11 females; mean age 37.8±28.4 years) with diagnosis of epilepsy, according to the ILAE criteria were included in the study. All patients underwent neurological, PET/CT, MRI, and EEG examinations. Interictal PET/CT images were acquired starting at 60 min after the i.v. injection of 5.0 mCi of (18) F-fluorodeoxyglucose (FDG).

Results: Neuroimaging showed abnormal findings in 9 patients (1 with gray matter heterotopia, 4 with brain tumors, 2 with brain abscess, 1 with cerebral infarction, and 1 with cerebral demyelination). Focal hypometabolism found in 13p agreed with the epileptic foci in 9 while 4 presented with larger hypometabolic areas. 2p had normal brain metabolism despite the EEG findings. Focal hypermatabolism corresponded to the tumor location in 3p with malignant brain tumors. Additional hypometabolic areas were observed in the surrounding regions, concordant with the neuroimaging findings of perifocal edema.

Conclusion: In this study the focal hypometabolic lesions observed by interictal FDG PET were the most responsible sites for seizures. Our results suggest that interictal FDG-PET/CT may be an important tool to better understand the neurobiology of seizures and to better define the ictal onset, functional deficit and surround inhibition zones in epilepsy.

Key words: FDG-PET, EEG, MRI/CT, epileptic focus, diagnosis

COINCIDENCE OF ANEMIA WITH MULTIPLE SCLEROSIS: RETROSPECTIVE ANALYSIS AND LITERATURE REVIEW.

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Background: An association of MS with different anemic syndromes, most often pernicious and Vitamin B12 deficit anemia has been reported. The role of Vitamin B12 in the myelin formation and its immunomodulatory and neurotrophic effects has been previously discussed. Accordingly, the coincidence of anemia with MS has been considered to impact seriously on clinical presentation, therapeutic strategy and patients' quality of life.

Objective: To perform a retrospective analysis of 18 cases with anemic syndrome as a factor of comorbidity in patients with MS.

Material and methods: 18 MS patients (15 women and 3 men) with RRMS (13), PPMS (2), and SPMS (3) diagnosed according to McDonald criteria were included in the present study. Average age was 36.4±8.5 (22-42) years, average disease duration 10.6±6.8 (4-18) years and means EDSS

3.5±2.5 points (2-6). 13 (72.2%) patients presented with anemic syndrome before the age of 40 years. All individuals underwent clinical, MRI, and complete hematological examinations.

Results: The study group included patients with pernicious (n=8), Vitamin B12 (n=6) and iron (n=3) deficit anemia, as well as with B-thalassemia (n=1). In 12 patients anemic syndrome proceeded MS and in 6 evolved during the course of the disease.

Conclusion: Our own notices and literature review suggests a possible causative relation between MS and anemic syndrome. The role of this coincidence on clinical presentation, necessity of additional treatment, and patient's quality of life is discussed.

Key words: anemic syndrome, MS, coincidence

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YOUNG ADULT SURVIVORS FROM CHILDHOOD CANCER FOLLOWED IN CHILDREN ONCOHEMATOLOGY AMBULATORY

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BACKGROUND: The objective of the current study was to describe a transition program for following children and adult survivors from childhood cancer in Children Oncohematology Ambulatory and to report the late toxicity effects diagnosed in all survivors.

METHODS: The population of the study comprised of children and adult survivors from childhood cancer (n = 253) who were examined in Children Oncohematology Ambulatory prior January 31st, 2010. The median age of the survivors was 16.20 years (range, 4-36 years) and the median interval from the time of cancer diagnosis was 8.7 years (range, 2-19 years). Primary cancer groups included: leukemia - 34%, non-Hodgkin lymphoma - 8%B, Hodgkin disease - 13%, Soft tissue sarcoma 12%, Neuroblastoma -

14%, Wilms tumor - 10%, and other - 9%. Late effects were described in range of systems.

RESULTS: Approximately 66% of the patients (168 of 253) had at least one late effect, 41% of patients had a single late effect whereas 12% had 2 late effects.

CONCLUSIONS: The current study represents an example of a successful multidisciplinary transition in an ambulatory, setting for children and adult survivors of childhood cancer. Late effects of cancer treatment are common in survivors, with approximately all human body systems involved: CNS 46%, Ototoxicity 15%, Cardiotoxicity 2%, Second malignenses 0,5%, Ocular 3%, Dygestive tract 5%, Immune system 3,5%, Lung 9%, Kidney 11%, Endocrine system 5%.

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