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“DO IT YOURSELF” PRINTERS IN ANATOMY EDUCATION

INTRODUCTION. Three-dimensional printing also known as additive manufacturing is a way to create 3D objects. The first stage in 3D printing is a computer-aided design (CAD) in which models are created from the ground up with 3D modeling software or on data generated by a 3D scanner. The printing is done by building up the object layer by layer under computer control. It is theoretically possible to get objects in any shape and form with precise details. Do it yourself (DIY) 3D printers are used for creating lifelike anatomical models which are more affordable alternatives to other artificially created models. Given the fact that hard tissues are the most suitable option to print, bones were a great first step to start off our project.

METHODS USED. Many additive processes are available. The main differences between processes are in the way layers are deposited to create parts and in the materials, that are used. There are some methods which work by melting or softening the materials for creating the layers. In this case, the model is formed by extruding small beads or streams of material. These methods are known as fused deposition modeling (FDM). A wide variety of materials are extruded, including acrylonitrile butadiene styrene (ABS), and polylactic acid (PLA), etc.

Other methods cure liquid materials. Solid parts are produced from liquids in stereolithography.

Printable models usually are created with computer-aided design or 3D scanning.

RESULTS AND CONCLUSION. In our case, 3D scanned bones were printed in high accuracy, exactly imitating the original sample. The upper limb bones (ulna and radius) were created with fused deposition modeling method using PLA as printing material. Furthermore, we are looking forward to the printing of other anatomical structures, particularly those that are difficult to observe and manipulate.

KEYWORDS:

3D printer,
anatomical models,
3D scan,
upper limb bones,
fused deposition modeling

SAFETY OF CYCLOSPORINE IMMUNOSUPPRESSED CANCER XENOGRAFT MODEL

INTRODUCTION. Cancer xenograft models are widely used in preclinical testings of drugs and studies of the tumor biological properties. Xenograft models correctly mimic tumor behavior, they are efficacious, cheap, and reproducible and cyclosporine immunosuppression is proven to have those advantages. Nevertheless, cyclosporine has a lot of side effects, among which there are nephrotoxicity, hepatotoxicity, cardiotoxicity, and neurotoxicity. The purpose of this study is to evaluate the side effects of the cyclosporine immunosuppression for cancer modeling.

METHODS USED. Adult albino rats weighing 100+/- 5 grams were immunosuppressed with cyclosporine 25mg/kg i/p 48h prior to surgery and during all the days of the experiment. The rats were anesthetized with Nembutal 40 mg/kg i.p. and were placed on the stereotactic frame. The tumor cells were injected subcutaneously. [3]The rats were sacrificed on the 10th day of the experiment when tumor growth was expressed grossly enough. The rats' organs were taken for morphological analysis.

RESULTS AND DISCUSSION. There was pericellular edema of neurons and reactive astrocytosis in the brain tissue. The lobar structure of the liver was preserved, the nuclei of hepatocytes were wrinkled, picnotic and dystrophic, with highly expressed nucleoli. Also, there were small regions of inflammation and spotty necrosis. The cerebellum remained without changes. The glomerules were hypercellular in the kidneys, and the tubules had not changed. The bowel and the mucosa also remained the same, the submucosa had an edema. There was another edema in the muscles of the heart. We took some blood from the heart for the analysis and that was the reason of the edema. In lungs there was emphysema, there was also a plasmocyte infiltrate in the interalveolar septum. In the blood vessels of the lungs, there was angiostasis. There was a secondary non-specific inflammation reaction. We can guess that it was the rats' response to the tumor. As the duration of the experiment was not very long and the morphological changes in the organs were not specific and fatal, so they can be tolerated.

CONCLUSION. Cyclosporine immunosuppression has some limitations due to its side effects but it still can be used for xenograft cancer modelling in rats.



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RELATION BETWEEN PEPTIC ULCER DISEASE AND COLORECTAL CANCER

INTRODUCTION. The peptic ulcer disease and colorectal cancer (CRC) are widely spread in Armenian population. However, the relation between peptic ulcer disease and CRC has been poorly investigated, and the findings are contradictory.

One of the mechanisms for colorectal carcinogenesis are microsatellite instability (MSI) and chromosomal instability. CRCs with a high level of microsatellite instability are clinicopathologically distinct tumors characterized by predominance in females, proximal colonic localization, moderate differentiation, mucinous histology, tumor-infiltrating lymphocytes, a Crohn's-like lymphoid reaction and a favorable prognosis.

Our goal was to investigate the association between peptic ulcer disease and CRC.

METHOD USED. This cross-sectional study investigated the relationship between prevalence of peptic ulcer disease in 359 CRC patients. We have randomly selected 30 cases for histological analyses. 30 formalin fixed, paraffin-embedded sections were stained by routine hematoxylin-eosin and Giemsa methods. We used appropriate methods for statistical analysis. A p-value of 0.05 was considered significant.

RESULTS AND DISCUSSION. From 359 patients who had CRC, 1,7% had a duodenal ulcer, and 11,4% had gastritis. 181 were female, 178 were male. The average age of the patients was 64,1532 [64± 8.06]. In histological features, it was revealed that 80% of all the investigated cases (24/30) mainly had cribriform growth pattern. Lymphoplasmacytic infiltration was present in 70% (21/30) cases. Acute inflammation and necrosis were revealed in 30% (9/30). The tumorous desmoplastic reaction was expressed in 12% of cases (4/30). Moderately differentiated adenocarcinoma was identified the whole investigated material. In 6 cases there was invasion to the muscularis propria (T3), in 15 cases there was invasion to the submucosa (T2), and the remaining material had just a mucosal involvement (T1). No spirally shaped structures were revealed by Giemsa staining. Although we have collected the data available almost in all Armenian major hospitals where CRC patients were treated, our data was not enough to show a significant correlation between peptic ulcer disease and colorectal cancer.

CONCLUSION: We could not find the correlation between peptic ulcer disease and colorectal cancer in our study. One possible reason is that CRC in Armenian population may be more correlated with other etiological factors, such as genetics and age. It is well known that microsatellite instability plays a huge role in the etiology of colorectal cancer and we have histologically received indirect signs that prove it. Therefore, we may assume that each person in Armenia who suffers from colorectal cancer should be verified for microsatellite instability, since the identification of its colorectal tumors is an important molecular marker, which lets us recognize the subgroups of patients with different phenotypic characteristics, survival and relapse rates.

A CASE REPORT OF LETHAL GUILLAIN-BARRÉ SYNDROME AND LITERATURE REVIEW

INTRODUCTION. Guillain-Barré Syndrome (GBS) is acute inflammatory demyelinating polyradiculoneuropathy (AIDP). The symptoms appear 2-4 weeks after relatively benign respiratory or gastrointestinal illness. The clinical manifestation of GBS is weakness, sensory changes, pain, autonomic changes, including also cranial nerves and respiratory system.

CASE REPORT. Previously healthy 63-year-old man was admitted to the hospital with a 3-day history of fever (39.5 oC), chills, sore throat and progressive ascending lower extremity weakness culminating in quadriplegia. The patient also had a cold, bee stinging a week ago and diarrhea 2 days before the symptoms appeared. No past medical history or family history was mentioned.

The initial examination revealed a decreased level of consciousness without meningeal signs, a reflex loss, tetraplegia without sensory loss, torpid limbs, limited movement of the eye to the outside, swallowing difficulty and pelvic autonomic nerves' dysfunction. Cerebrospinal fluid examination showed increased protein concentration with no cells found. The Electroneuromyography of the nerves of the bilateral lower and upper extremities found severe, generalized, motor peripheral neuropathy of the predominantly demyelinating type, with an axonal component. It corresponds to the pure motor axonopathic variant of GBS (acute motor axonal neuropathy (AMAN)).

Clinical findings, electrodiagnostic studies and cerebrospinal fluid results were classically associated with Guillain-Barré syndrome, demyelinating type.

The clinical symptoms continued to progress on the 7th day after symptom onset although immunosuppressive therapy and plasmapheresis were initiated. His neurological status rapidly deteriorated. After about three weeks after he was admitted to the hospital the patient died of ventilatory failure. Pathological diagnosis confirmed acute polyradiculopathy, Guillain-Barré syndrome. The lung examination showed respiratory failure.

DISCUSSION. Guillain-Barré syndrome is usually non-fatal and can be well managed via supportive care, intravenous gamma immunoglobulin, and plasmapheresis, which are proven to improve complications and mortality. It causes death only in 2-4% of cases. Although all the required treatment options have been implemented in this clinical case, the patient has died due to progressive disease and respiratory failure. This indicates that further research and investigations are needed to improve treatment modalities. For example, it is known that both arms of the immune system are involved in the pathogenesis of Guillain-Barré syndrome and stimulate macrophages that act against the peripheral nervous system. On the other hand, both gamma immunoglobulin injection and plasmapheresis mostly effect humoral immunity. Still, the steroid therapy has not improved the outcome of the disease in clinical studies. Now, the anti-macrophage therapy for cancer in murine models is widely investigated. Possibly, this treatment option can also improve the outcome of Guillain-Barré syndrome, which is resistant to the approved treatment plan.

CONCLUSION. Although all the required measures were implemented, the Guillain-Barré syndrome was lethal for the patient. That indicates the shortcomings of the approved treatment modalities and need for improvement of the pathogenetic treatment.



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A CASE REPORT OF STRUMA OVARIII AND REVIEW

INTRODUCTION. Struma ovarii is an ovarian teratoma, which mainly contains thyroid tissue. Struma ovarii can be of different sizes, but usually, it is a mature mass below 10 cm in diameter. The thyroid tissue in struma ovarii is identical to thyroid tissue from both biological and microscopical points of view. The symptoms of struma ovarii are palpable lower abdominal mass, lower abdominal pain, abnormal vaginal bleeding, ascites, hydrothorax, elevated thyroid function. In many cases, patients with struma ovarii are asymptomatic.

CASE REPORT. A 60-year-old woman complained of a large pelvic mass. She had only one child and she was in menopause. Laboratory results of biochemical analysis and pre-operative tumor markers were unremarkable. From her past medical history, a cardiologist suspected thyroiditis but she refused to undergo further investigation. Her current physical examination was normal, except for the palpable, painful pelvic mass. She underwent surgery for right umbilical hernia repair and right ovarian cystectomy. Histology reported a mature teratoma - struma ovarii and chronic salpingitis.

DISCUSSION. After reviewing the patients with struma ovarii we have discovered that this disease takes some efforts to be diagnosed through clinical manifestations or imaging studies because of the diversity of its clinical features. It is sufficient to treat by surgery as it is in case of dermoid tumors for benign lesions, and even if there are secondary complications, most often they regress impulsively after removing the primary tumor. The optimal treatment modality is difficult to determine considering both the advantages and the risks of less aggressive treatment in the context of little evidence. Serum thyroglobulin level gives useful information for making the diagnosis, serving as a sensitive tumor marker during clinical monitoring of the disease status or activity in malignant struma ovarii as well as in thyroid carcinoma. The treatment for struma ovarii can be bilateral oophorectomy. The contralateral ovary is removed because of the 10% chance of a contralateral teratoma. Fertility-sparing treatment is also an option but patients should be selected carefully according to their condition.

CONCLUSION. Struma ovarii is a rare tumor with different clinical symptoms. Symptoms include hyperthyroidism, can mimic malignant ovarian tumor, and it also can be asymptomatic. The correct diagnosis is essential for premenopausal women and determines the management and prognosis of the patient. Struma ovarii is important to be considered while the differential diagnosis of hyperthyroidism.

KEYWORDS:

*Struma ovarii,
Ovarian teratoma,
Hyperthyroidism.*

THE IMPACT OF HIGH-FAT DIET AND RESTRICTED PHYSICAL ACTIVITY ON RAT BEHAVIOR

INTRODUCTION. Nowadays obesity is a public health issue worldwide. According to the data from The Global Burden of Disease (GBD), more than 12% of adults and 5% of children suffer from obesity. High body mass index (BMI) is associated with such chronic diseases as type 2 diabetes mellitus, cardiovascular disorders, several types of neoplasms, non-alcoholic fatty liver disease. In recent years, studies confirm the relationship between obesity and mental illnesses like schizophrenia, bipolar disorder, depression, and dementia. An “obesogenic” environment, which includes consumption of high-calorie foods and reduced physical activity, might lead to the impairment of learning and memory. In our previous studies, we evaluated the influence of restriction of movements (hypokinesia) on behavioral changes in rats. In this work, we applied a diet-induced obesity model in conditions of restricted physical activity to investigate the correlation between obesity and behavioral changes including locomotion, motor coordination, and memory.

METHODS USED. Male albino rats (10 weeks old) were housed in a controlled environment with free access to food and water. Animals with satisfactory results in the open field pretesting were included in the experiment. The rats were randomly assigned into 4 following groups: 1. Rats fed a high-fat diet with restriction of physical activity. 2. Rats fed a high-fat diet without restriction of physical activity. 3. Rats fed a low-fat diet with restriction of physical activity. 4. Rats fed a low-fat diet without restriction of physical activity, control group. The high-fat diet contains 24g of fat/100g food and low-fat diet contains 4g of fat/100g food. The physical restriction was achieved by housing the animals in narrow cages (plexiglass, size: 20*7*7 cm³) for 22 hours per day. The duration of the experiment was 70 days. The weight gain of the animals was monitored by weighing twice weekly. At the end of the 5th week as well as at the end of the 10th week, some behavioral tests were applied (Open field exploration test and Novel object recognition test). Behavioral trials were recorded and analyzed by Any-maze software.

RESULTS. There is a statistically significant difference in weight gain between high-fat fed and low-fat fed animals ($p < 0.01$), which means that a chosen model was correctly applied as an obesity model. Novel object recognition test, which was conducted at the end of the experiment, showed some memory impairment in rats fed high-fat diet and housed in narrow cages comparing with the control group ($p < 0.05$). In the open field test results, the expected difference in locomotion was not observed. However, some specific parameters, like grooming frequency and duration, must be mentioned. Physically restricted high-fat fed rats show longer and more frequent grooming compared to the physically restricted low-fat fed rats ($p < 0.05$). This parameter is mostly associated with instability of emotional status and might be interpreted as an indicator of chronic stress.

CONCLUSION. The given data proves that obesity has its own impact not only on metabolic changes but also on behavioral status. For further study of obesity-induced behavioral changes more specific tests should be applied.



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CONCLUSION. The given data proves that obesity has its own impact not only on metabolic changes but also on behavioral status. For further study of obesity-induced behavioral changes more specific tests should be applied.

A CASE REPORT OF NONSECRETORY MYELOMA

INTRODUCTION. Nonsecretory myeloma (NSM) is a type of plasma cell neoplasm. Whereas classic multiple myeloma secretes of abnormal immunoglobulin that can be detected in blood and urine, NSM does not cause monoclonal gammopathy. In both cases, the clinical and imaging features are essentially similar.

The definitive diagnosis is made according to the immunohistochemical picture of bone biopsy. NSM is associated with the same renal, hematologic, bone complications, such as renal insufficiency, anemia, bone marrow failure, infections, pathologic fractures, spinal cord compression, hypercalcemia, spinal cord and nerve root compression.

CASE REPORT. A 61 year- old man was admitted to the hospital with complaints of lumbar pain. A year ago he was treated for high blood pressure and hypercreatininemia. At the time of being admitted to the hospital, his complaints were also a headache and general weakness. The laboratory analysis revealed anemia, thrombocytopenia, as well as high creatinine, ASAT, ALAT and bilirubin levels.

CT revealed multiple destructive foci of the skull, ribs, vertebrae, both collarbones, shoulders and pelvic bones, subpleural shadow foci of lungs, fibrosis in both lungs, pneumocele in the lower lobe of the left lung, the curvature of the nasal septum, atrophy of the brain and calcination of the aorta wall. He was treated in nephrology department for 10 days, without hemodialysis.

After the treatment, he was admitted to another hospital with pain in the left part of the chest. A trepanobiopsy of the hipbone and the sternal puncture was conducted with no further complications.

Immunohistochemical analysis revealed hypercellular bone marrow with myeloid and megakaryocytic cells. There was interstitial infiltration with monomorphic cells, with hyperchromic nuclei, and eosinophilic cytoplasm. The histological picture and immunohistochemical analysis showed a plasma cell leukemia. KI67, CD15, CD20, CD34, CD61, CD117, MUM1, KAPPA, OCT2, MYELO were positive.

After hematological consultation, the patient started chemotherapy, but required hemodialysis due to renal failure and has died after two days. Pathological examination confirmed general (diffuse) form of the myeloma disease associated with osteoporosis. Complications were the para-amyloidosis of the kidneys, heart, liver, chronic kidney failure, anemia, and pneumonia. The reason of the death was the progressive multi-organ failure.

DISCUSSION AND CONCLUSION. The absence of paraprotein in the blood does not exclude multiple myeloma. Though doing a bone marrow biopsy routinely in all cases with suspected multiple myeloma can put extra strain on the hematology department, we recommend consultation with hematologist when the diagnosis of multiple myeloma is strongly suspected, in the absence of any abnormal protein in blood and urine, to avoid delay in diagnosis. We also suggest pooling of tissues of rare cancer in biobanks for future research. Molecular and genetic studies can be performed to help us understand their behavior.

Patients with multiple myeloma often present with vague, common symptoms such as back pain, bony pain, fatigue, and anemia. Differentiating multiple myeloma from other causes of back pain is especially important in making management decisions. The confirmation of diagnosis rely on diagnostic criteria for multiple myeloma. Multiple myeloma is frequently accompanied by a poor prognosis, but early-onset cases generally respond more favorably to interventions.



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Machine learning,
Signal processing

CONTROL OF A CUSTOM BIONIC HAND WITH MACHINE LEARNING DATA ANALYSIS

INTRODUCTION. Basic artificial limb substitutes have been used since 600 BC. They were simple structures made of wood or metal to resemble limb movement. Over the past 30 years, there have been drastic improvements in the field prosthetic technology. At the moment bionic hands can grasp and manipulate objects, with added features to enhance their performance, as opposed to poor substitutes of limbs that were available before. For the modern prosthetics, it is significant to have biocompatibility as they have to respond to commands from the nervous system and replicate authentic movements. Companies are trying to make bionic hands with a sense of pressure, temperature, pain, etc. Modern bionic hands are capable of recreating the functionality and range of motion experienced by a healthy limb. Researchers are also succeeding at the aesthetics. Some of the bionics available in the market are being created to resemble the actual human at the highest level. Nowadays, there are different types of commercial bionic hands in the market, which support various functions depending on the price. Nevertheless, there is still a need of affordable high-quality limb prosthetics, which can be precisely mind-controlled as it requires less adaptation time, is non-invasive and more comfortable.

As there are thousands of people with upper limb amputation in our region, there is a need of high-quality limb prosthetics is to them. Our goal is to improve the quality of affordable limb prosthetics, especially for low-income countries which suffer from war and natural disasters. The main objective is to develop a mind-controlled bionic hand and improve the brain-machine interface with the use of machine learning tools for EEG data analysis. In addition, we design the artificial skin or glove using the 3D scanning, modeling and printing techniques and the pigmentation of the artificial skin will be similar to the real one. As a result, our prosthetics can be adapted on several levels.

METHODS USED. The methodology includes the following processes: Limb assembling, EEG recording, data analysis and limb control using the data. The first part includes the 3D scanning of the spared limb, 3D modeling of bionic one (using 3Ds MAX), 3D printing and assembling of the parts. EEG recording and data analysis are conducted as described in Young et al., 2015 and Venthur et al., 2015 with further development of methodology.

RESULTS. A 3D printed bionic hand, which is based on the scan of the spared hand 3D reconstruction has been designed. The hand can be controlled by EEG data analysis using Python machine learning algorithms.

CONCLUSION. With the help of the bionic hand, a disabled person can have the feeling of control over his artificial bionic hand, in the same way as in their biological one. This is a huge benefit to both the individual and the society. The patient will restore the functionality and improve the quality of life. In addition, the analysis tool can also be used in augmented reality games for the limb movement by the will.

INVESTIGATION OF ULCEROGENIC ACTIVITY OF ARYLPROPIONIC ACID DERIVATIVE

INTRODUCTION. Development of a new agents with analgesic properties among nonsteroidal anti-inflammatory drugs remains important field in drug discovery taking in account wide range of their side effects, including gastrointestinal disorders. New compounds with anti-inflammatory and antinociceptive activity was obtained among derivative of arylpropionic acid from non protein amino acids (NPAA). In previous investigations it was demonstrated that S(-) – 2 amino – 2 – methyl – 3 – phenylpropanoic acid (NPAA – 36) decreased formalin-induced inflammation in rats (1) and increased latent time in Tail flick model of nociception measure (2). For further development of mentioned compound as a potential non steroid anti-inflammatory agent it was important to investigate its ulcerogenic property and compare with the same action of Ketoprofen as a structure analog with improved effectiveness.

METHODS USED. Experiments was carried out in 24 adult male albino rats weighing (180-200 g), kept at standard laboratory vivarium conditions. Animals was divided into 3 groups by 8 rats in each. The rats were fasted for 18 h prior to the experiment. After that animals of group 1 which served as a control received only 0,5 ml distilled water once a day during 2 days. Rats from group 2 and group 3 received Ketoprofen and NPAA-36 accordingly at the same regimen, in dose 50 mg/kg by oral gavage needle. After 7 h of the last dose, all rats were sacrificed. The rats' stomach were excised, opened along big curvature and washed with saline. Stomachs were examined for damaged surface in by program Image J.

RESULTS. Conducted investigation evident, that Ketoprofen disturbed mucosa completeness of stomach by $2,06 \pm 0,569\%$ ($15,87 \pm 5,77$ mm² damaged from $761,19 \pm 133,35$ mm² of total stomach surface). In spite of Ketoprofen caused changes administration of NPAA-36 didn't induce any essential deviations compared with the control group of rats: just in some cases was observes the week and rare redness.

CONCLUSION. Thus investigated derivative of arylpropionic acid from non-protein amino acids in dose 50 mg/kg appear anti-inflammatory and antinociceptive activity without disturbance of stomach mucosa and can be sources for new anti-inflammatory drugs with fewer side effects. Mentioned differences of gastrointestinal action of investigated amino acid probably are due to the presence of additional amine group in structure as it has been postulated, that masking the acidic properties of NSAIDs by insertion of the nitrogen-containing group leads to decrease the gastrointestinal toxicity through the falling of pH.



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THE MERCHANDISING ANALYSIS OF SEVERAL VOLATILE OIL CONTAINING PLANTS

INTRODUCTION. Herbal origin drugs are used more often in recent years. In 1997 only 14% of US population used phytopreparates, and in 2005 – 55%. In European countries 20% of pharmacy assortments are herbal preparations [1]. It is considered traditionally, that herbal origin drugs are less dangerous and don't produce serious side effects. In directories there is a lot of information about plants used in the treatment of a range of diseases, but no information about the quantity of active compounds and clinical researches. The aim of this work is standardization of herbal raw materials according to quality indexes. Thyme crawling is evergreen semi shrub and is met in forests. The crude drug for Sage is leaf, which is elongated oval and silvershining. Above mentioned plants belong to Lamiaceae family [2]. Thyme crawling contains cymol, thymol. It is expectorant and spasmolytic. Thyme volatile oil is antibacterial, anti-inflammatory, antiseptic. Sage contains cineol. It produces anti-inflammatory effect and is used in dentistry.

METHODS USED. As a material herb of Thyme crawling and Sage leaves are used harvested in July of 2017. The analysis was carried out according to merchandising methods [2,3,4]. This method was chosen for herbal raw materials standardization.

RESULTS AND DISCUSSION. The anatomical-distinctive features of above mentioned plants were determined. In merchandizing analysis quality indexes of Thyme crawling and Sage were defined. Ash for Thyme is 8% (not more than 12%, according to SPh) moisture: 7.2% (not more than 13%, according to SPh), extracting substances 19.7% (not less than 18%, according to SPh). And for Sage ash is 7% (not more than 12%, according to SPh), moisture – 2.4% (not more than 14%, according to SPh), volatile oil – 0.94% (not less than 0.8%, according to SPh).

CONCLUSION. The results of analysis define the identity of herbal raw materials and showed that results satisfy the demands of SPh.

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A CASE REPORT OF MITRAL VALVE REOPERATION DUE TO ACUTE MITRAL VALVE DYSFUNCTION

INTRODUCTION. Mitral valve (MV) dysfunction causes heavy symptoms and many complications. MV reoperation has high-risk probability. The purpose of this study is to evaluate the risks of MV reoperation and expected outcomes ratio of this case to the literature review.

CASE REPORT. A 52-years old female was admitted to hospital in severe condition, with pale skin color and excessive sweating. The patient had complained of dyspnea, orthopnea, cough, and hemoptysis for 4 days. History mentioned mitral valve prosthetic, pulmonary veins isolation, thrombus removal from left atrium due to rheumatoid mitral stenosis. Blood pressure was 150/80, Ps 130, and SaO₂ was 78%. Wheezes were heard from both lungs. The left atrium was enlarged, Left and right ventricles showed normal contraction. Mitral valve inflow was 3.5/3.0 m/m, and Pmax mean was 48/40 mmHg. Mitral regurgitation stage was III0, tricuspid regurgitation stage was II -III0. In pericardium, no fluid was identified. A moderate fluid was in the pleural cavity.

The diagnosis of acute heart failure, pulmonary edema, and atrial fibrillation was confirmed. Post operation and anticoagulation therapy were increasing the risk.

On the preoperative day, the patient had adverse status, the edema was increasing, and saturation decreased to 80%. ECG revealed mitral prosthetic dysfunction due to thrombosis. The patient was transported to OR.

The patient was intubated and arterial catheterization (BP≈40 mmHg). Urgent sternotomy was conducted. Aorta, inferior and superior vena cava were cannulated and artificial blood circulation (ABC) was started. Body temperature was decreased to 28 0C. Aorta was clamped and injected with a cardioplegic solution. Then the left atrium was approached and thrombus was removed.

The left atrium was sutured, ABC was removed and vessels decannulated. After hemostasis thorax was closed.

On the first postoperative day, the patient was on mechanical ventilation. Hemodynamic indicators were the following: Blood pressure-110/60 mmHg, Ps-89 b/m, SaO₂ -90%, CVP-5 mmHg. Patient breathed independently for 5 hours.

CONCLUSION. The patient who underwent mitral valve prosthetics has the probability of mechanical prosthetics infection, which complicates the process bringing to acute heart failure. Critical status of the patient requires surgery although the risks. Thereby, reoperation of mitral valve surgery is being performed in increasing numbers possibly with a superior result which was shown in this case.



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mTOR AS A POSSIBLE TARGET FOR ASD PHARMACOTHERAPY

INTRODUCTION. The core independent symptoms of autism are difficulty with social interaction and communication, repetitive behavior, interests, and activities. Under term “syndromic” autism stands autism with another clinical signs or conditions, with known genetic causes. Chromosomal abnormalities, submicroscopic copy number variations, and mutations in a single gene are considered as etiological factors for various syndromic autism disorders. Monogenic ASDs are detected in 3-5% of subjects with ASD. In nonsyndromic autism, no additional symptom presents besides of classical autism symptoms, and very few are known about etiology for most cases of nonsyndromic autism. About 90-95% of individuals having autism are diagnosed with nonsyndromic autism. Despite the heterogeneity of syndromic ASD common affected cell signaling pathways could be key to understand of the pathogenesis of autism and define the target for treating autism. mTORC1 signaling pathway in autism spectrum disorder the tuberous sclerosis complex (TSC) can open new insights in evaluating the role of mTOR in neural development. It is caused by loss-of-function mutations in the genes encoding TSC1 or TSC2. One of the results of this mutation is disinhibition of Rheb and overactivation of mTOR. This dysregulation of mTOR leads to abnormal brain development. Morphologically TSC is presented by tubers, white matter heterotopias, radial migration lines, and subependymal nodules and which is more specific for autism reduced or dysmorphic dendritic spines. Phosphatase and Tensin Homolog-Associated ASD loss-of-function mutation also brings to overactivation of mTORC1 through constitutive activation of downstream AKT/mTORC1 pathways. In Neurofibromatosis Type 1 it was shown that upregulation of mTORC1 is resulted by AKT/mTORC1 dependent but TSC/Rheb independent manner. The dysregulation of mTOR pathways also can be seen in Fragile X, Angelman and Rett syndromes but findings are not as certain as in disorders described above. Hyperactivation of mTORC1 pathway was observed in postmortem brains from adolescent patients with idiopathic ASD and was shown to impair autophagy and spine pruning during childhood and adolescence, leading to increased basal dendritic spine density and, therefore, enhanced excitatory connectivity. In mouse models of TSC treatment with rapamycin was effective in diminishing tumor size in lungs, kidneys, and brain in patients with TSC, and in improving specific cognitive functions.

METHODS USED. In this review we analyzed 20 articles indexed in Web of Science and Scopus, which have an impact factor by Thomson Reuter

CONCLUSION. The pathogenic targeting and pharmacotherapy research is mainly based on genetic models of monogenic autism spectrum disorder. The studies on genetic mouse models of monogenic ASDs shows that targeting even indirect pathways of AKT/mTOR signaling leads to mitigation of autism-related symptoms. In the case of the most characterized monogenic disorder TSC it was shown the role mTOR signaling pathway in the development of the disease and effectiveness of mTOR targeting therapy for removing autism-related and nonrelated symptoms. mTOR signaling is a major regulator of cell metabolism and targeting of mTOR allows to alter various metabolic processes at once, so it should be considered in the future research of ASD pharmacotherapy.

TOTAL MESORECTAL EXCISION WITH FORMATION INTERSPHINCTERIC HAND-SEWN COLOANAL ANASTOMOSIS AND PREVENTIVE TRANSVERSE COLOSTOMY

INTRODUCTION. Colorectal cancer is the third leading cause of death worldwide. The most common form of colon cancer is adenocarcinoma. Colorectal cancer metastases are most commonly found in the liver, and the lung is the second most common site. As the disease progresses, symptoms may present with constipation or diarrhea, rectal bleeding, persistent abdominal discomfort, meteorism, pain, unexplained weight loss. The treatment of rectal cancers is multimodal, with adjuvant radiotherapy and chemotherapy having benefits in some settings. Total mesorectal excision is a common procedure used in the treatment of colorectal cancer in which a significant length of the bowel around the tumor is removed. The number of metastases is an independent prognostic factor in the surgical treatment. Resection of isolated pulmonary metastases can increase survival rates up to 40% at 5 years. Nevertheless, pulmonary formations can be turned out to be due to a benign disease and in which the treatment of choice would not be surgery, as in our case.

CASE REPORT. The patient is a 64-year-old male with a past medical history of hemorrhoidectomy in and TUR for bladder cancer, recently presented with rectal bleeding and chronic constipation.

A bleeding tumor was revealed with a digital rectal examination. It was 5 cm above the anus, mainly on the posterior and left walls.

CT chest/abdomen/pelvis: On the left semicircle of the lower-middle-ampullar part of the rectum, a "saucer-shaped" tumor, 4.0cm in length, 13mm in thickness, was revealed. The tumor infiltrates the left wall of the rectum, leaving intact the right hemisphere, there is no narrowing of the lumen of the rectum. The lower edge of the tumor is located at the distance of 6.0cm from the edge of the anus. The outer contour of the affected wall is clear, the pararectal tissue is not infiltrated, the mesorectal fascia is intact, not thickened. Para-rectal to the left a single lymph node, 10mm in size, was detected. Inguinal, iliac and para-aortic lymph nodes were not enlarged. In the subpleural parts of the S9 segment of the left lung, a focal formation of 13 mm in size is defined. In the basal parts of the tongue segment, a second focus, 10mm in size, was identified. The first probably benign, the second can be metastatic.

The patient was operated: total mesorectal excision with formation intersphincteric hand-sewn coloanal anastomosis and preventive transverse colostomy.

Pathohistological examination detects moderately differentiated rectal adenocarcinoma, WHO ICD O-code 8140/3, pT2pN1pMx R-/negative/, Grade 2.

After patient received 6 courses of chemotherapy (FOLFOX 6).

During follow-up, clinical examination, and CT scan no signs of continued neoplastic growth within the chest, abdominal cavity and pelvis were revealed. Foci of the left lung in dynamics without changes-probably benign genesis (adenoma or hamartoma).

CONCLUSION. There was an increasing trend toward sphincter-preserving procedures for the treatment of low rectal cancer. Intersphincteric resection with hand-sewn anastomosis and postoperative radiotherapy were independent risk factors of anastomotic stricture. And despite this, our patient shows favorable clinical outcomes. Our case proves that this technique is an acceptable alternative to traditional procedures. Besides our case shows that riskiness of surgery can be justified in colorectal cancer and that probability of metastasis is not an absolute contraindication for surgery.



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THE ANALYSIS OF SOME HERBAL RAW MATERIALS QUALITY INDEXES

INTRODUCTION. There is a large number of publications in world literature during recent 20 years about herbal raw materials' efficacy, safety, pharmacological activity and standardization. This process is especially active in EU countries, where Eph is periodically refreshed. Unfortunately the results of those publications are not estimated in domestic medical literature [1]. Calendula is rich in carotenes and vitamins. It is used in the treatment of gastrointestinal diseases, as well as in the treatment of wounds and skin inflammations. Rose is a source of vitamin C and is used to increase resistance of organism and to stimulate immune system. Marshmallow is mucilage containing plant. It covers mucous membranes and produces anti-inflammatory activity.

The aim of this work is a phytochemical and merchandising analysis of the above mentioned plants. Calendula is decorative annual plant with 30-50 cm height: contains carotenes, amount of which is up to 3%. Rose is a thorny shrub. Crude drug is fully ripen solid fruits, which contain large amount of ascorbic acid. Marshmallow roots, which have longitudinal wrinkles, contain polysaccharide, generally mucilage [2].

MATERIALS AND METHODS. As a material for research Calendula flowers, Marshmallow roots and fruits of Rose hips are served, harvested in July of 2017. The research was carried out by phytochemical analysis methods [2,3,4]. Carotenes were determined in Calendula officinalis flowers by spectroscopy method.

Vitamin C was determined in Rose hips by titration method. Mucilage was determined in Marshmallow roots by gravimetric method.

RESULTS AND DISCUSSION. The results of analysis define the identity of the raw materials and showed, that that results satisfy the demands of Pharmacopeia. The anatomical-distinctive features in the above mentioned plants microscopic preparations were determined. The quantity of carotenes in Calendula were determined by the method created by us. The quantity of carotenes in Calendula flowers (1.33%). The quantity of polysaccharides in Marshmallow roots and ascorbic acid in Rose hips were determined by Pharmacopeia. Polysaccharides in Marshmallow roots (13.3%) and ascorbic acid in Rose hips (1.33%) were defined. The quality indexes of above mentioned plants (ash, moisture, active compounds) were defined in merchandising analysis. The results satisfy demands of Pharmacopeia [4].

CONCLUSION. Calendula may be used as antioxidant due to carotenes. Marshmallow due to polysaccharides content may be used for upper respiratory inflammations. Rose hips may be used in the prophylaxis of cold and flu.

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ISCHEMIA-INDUCED NEURONAL CHANGES MAY BE GUIDED BY PHYSICAL ACTIVITY

INTRODUCTION. Although there are many studies concerning further changes following acute focal cerebral ischemia, very small data is available on the damage induced by chronic cerebral ischemia. Vascular cognitive impairment and dementia (VCID) is the clinical sign of chronic cerebral ischemia. Because of its variations, animal models have been developed to study multiple forms of VCID. In addition, researchers have shown that pathological lesions after unilateral common carotid artery occlusion (UCCAO) share common features with VCID. Some of the researchers suggest that physical activity has a positive effect on blood flow and brain function. The aim of the research was to gain up-to-date information on how physical activity can impact on ischemia-induced changes after UCCAO.

METHODS USED. The effects of swimming training (ST) on recovery after UCCAO was investigated in sedentary (N= 8) (control group) and trained (N=8) (experimental group) rats. By midline cervical incision, the right common carotid artery (CCA) was isolated from the adjacent vagal nerve and ligated. ST was performed on the third day after UCCAO in an apparatus adapted for rats. It contained warm water (30-32°C) and had a depth of 50 cm. The training protocol was conducted during the same period of the day (2:00-4:00 pm) for all the training sessions. During the first week, the swimming period was increased daily until reaching 15 min at the end of the fifth day. From the second week, the exercise duration was kept constant (15 min/day, 5 days/week) with 2 days of rest. This was maintained until the end of the training period, which lasted 3 weeks. After daily ST procedure, the animals of this experimental group were placed in specifically designed cages with the availability for free training on wheels. The behavioral assessment was performed in all groups. To evaluate non-spatial working memory related to frontal-subcortical circuits, an object recognition test and Y-maze spontaneous alternation test were performed. The brain tissue was taken for morphological analysis. The samples were stained with hematoxylin-eosin (H&E).

RESULTS. The morphological as well as behavioural results have shown that early activation after UCCAO can lead to the faster recovery in comparison with the sedentary group.

Morphological results. Neuronal death as well as cellular edema and astrogliosis are the main characteristics of ischemia-induced neuronal changes. These parameters are less expressed in the experimental group, which proves the neuroprotective role of early physical activity.

Behavioural test results. According to results obtained from experimental data, there were no significant changes in novel object recognition task parameters in the experimental group in comparison with the control group. Although spontaneous alteration as well as locomotor activity improvement was seen in the experimental group, however, it wasn't significantly different from baseline levels.

CONCLUSION. Concluding, we can say, that physical activity has a certain impact on further changes followed by ischemic processes. Some sensitive tests, like two-photon life imaging and electrophysiological studies, are needed for comprehensive investigation of brain morphologic and functional changes induced by physical activity.



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THE STANDARDIZATION OF EVERLASTING FLOWER (HELICHRYSUMARENARIUM L. MOENCH)

INTRODUCTION. Recently, the plants of Armenian flora which are registered in the state pharmaceutical documents have become very important. Climate conditions of RA have a great influence on the physiological and phytochemical parameters of herbal drugs. From this point of view the Everlasting flower (*Helichrysumarenarium* L. Moench.), which is widespread in Armenia, is remarkable. The herbal drug is the flowers which were collected from widely growing perennial herbs, before there were fully opened. The herbal drug contains naringeninflavone and its monoglycosideisosalypurposide, apigenin flavone and campheroleflavonol. The plant possesses anthelmintic activity, stimulates bile secretion. Fluid extract and drug “Flamine” are used in the treatment of liver and gallbladder acute and chronic diseases. The aim of this work is standardization of Everlasting flower according to the biological active compounds: sum of flavonoids in order to define its accordance to SPh XI.

MATERIALS AND METHODS. The herbal drug is the flowers of *Helichrysumarenarium* which have been collected from Voghchaberd region.

The water loss percentage was determined under the temperature 105°C in the drying case.

The total ash was determined in a muffle furnace (model MП-2YM).

The sum of active substances (flavonoids) was determined according to the quantity of isosalypurposide by the method elaborated by our group with the help of spectroscope (UV-VIS). Microscopic examination was carried out with the help of microscope (model Micros 10x40) [1].

RESULTS AND DISCUSSION. The results of experiments were the following water loss percentage – 11.2% total ash – 8 % the sum of active substances (flavonoids according to the quantity of isosalypurposide) – 2.4 %.

The results were compared to the data of SPh.

CONCLUSION. The results were compared to the monograph of Russian Pharmacopeia 11th edition and according to that, water loss percentage and total ash correspond to the monograph, on the other hand the total sum of flavonoids was 3 times less than it was mentioned in monograph [2]. The amount of flavonoids in Everlasting flower which grows in Armenian flora is behind of the amount of flavonoids mentioned in Russian Pharmacopeia. The probable reason might be not correct harvest period or the amount of flavonoids is low because of the climatic conditions in Armenia.

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A CASE REPORT OF CAROTID ARTERY BIFURCATION ANEURISM SURGERY

INTRODUCTION. Carotid artery aneurysms are rare but have a major role in ischemic stroke etiology. The causes include congenital factors, trauma, fibromuscular dysplasia, atherosclerosis, infections (tuberculosis, syphilis) and radiation. We report a case of carotid artery bifurcation aneurysm and review the literature on the treatment of this condition.

CASE REPORT. A 65-year old man was referred to the Vascular Surgery Department with a mass on the anterior surface of the neck, fatigue, and shortness of breath. He had a history of renal failure for which he was having hemodialysis for 5 years.

Investigations included a Doppler sonogram, which revealed the “mass” to be a 37x33 mm saccular aneurysm, a gap in the region of common carotid artery bifurcation to the external carotid artery and defect of the middle layer. CT demonstrated right (C3-C4 vertebral level) saccular aneurysm (axial 3.0x2.6 cm, horizontal 3.9x2.8 cm). ECG suggested left ventricular hypertrophy, and left ventricular failure. Atherosclerotic changes of aorta and valve were revealed. The comorbidities increased the risk of surgery. However, giving consideration to rupture of an aneurysm and thrombotic complication, surgery was conducted.

An approach was made to the common carotid artery (CCA). Aneurysmal sac was mobilized, internal and external carotid arteries were exposed from the sac. After administering 5000 units of Heparin intravenously, CCA, ICA & ECA were clamped, aneurysmectomy was performed. The anterior wall of sac was sheared off.

ECA was ligated and double sutured. PTFE prosthesis was inserted between ICA & ECA. After arteriotomy, the internal shunt was performed for prophylactic measures of stroke. The patient was transported to reanimation department without extubation. 7 hours after surgery, cardiac arrest was noted for 3 minutes, 0/0 pressure. After reanimation measures were taken, heart function was restored, sinus rhythm 140/90 pressure. There were infarction symptoms at day 1 after surgery. Troponin level was 2000. Coronography and right intraventricular artery stent were performed. 3 days later patient died due to cardiopulmonary failure. Pathoanatomical results showed recent transmural infarction area, left pleural effusion and pneumonia.

CONCLUSION. Most common symptom during CA aneurysm is neck deformation which was noted in this case, also neural deficits in the result of direct compressions such as of vagus, glossopharyngeal, hypoglossal nerves or Horner’s syndrome due to compression of the cervical sympathetic nerves. diagnosis may be established by Doppler ultrasound and CT angiography. Most common surgical treatment is aneurysmectomy and arterial restoring. Small aneurysms may be excised and the resultant defect closed primarily with sutures or repaired with a vein patch graft. Alternatively, the artery may be repaired by arterial ligation or end–end anastomosis. Where tension–free anastomosis is impossible PTFE or Dacron may be utilized. Surgical treatment remains high risk with notable complications including cerebrovascular accidents (4-4.5%) and death (50% in emergency cases). Shunts may be utilized in order to reduce the period of cerebral hypoxia, which was performed in this case. The role of endovascular techniques in the treatment of ICA aneurysms is not yet established.

Studies report recurrence of aneurysm after 19 years.



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