# INTERNAL DISEASES

# BRUGADA SYNDROME A SCIENTIFIC OVERVIEW

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## ABSTRACT

**Introduction: First described in 1992 by the Brugada brothers, Brugada syndrome is channelopathy of the sodium channels in the heart. It is a genetic disorder, over 60 different mutations have been described so far and at least 50% are spontaneous mutations, but familial clustering and autosomal dominant inheritance has been demonstrated. Brugada syndrome is associated with a high incidence of sudden cardiac death in patients with structurally normal hearts.**

**Materials and Methods: The information for this scientific overview was gathered using the search platform of PubMed and using the keywords: Brugada Syndrome, sudden cardiac death, arrhythmia, channelopathy, electrophysiology, risk stratification. The five articles used in this review have all been published after year 2010.**

**Results: Diagnosis is based solely on a specific but labile pattern on an electrocardiogram, defined as a ≥0.2 mV coved-type ST-segment elevation in the right precordial leads. However, the ECG can be silent, requiring sodium blockers to unmask the pathology. This electrocardiographic abnormality must be associated with clinical criteria to make the diagnosis. Electrophysiologic study is used to assess risk of sudden cardiac death no other risk stratification parameter is presently available for asymptomatic individuals.**

**Conclusion: Brugada Syndrome is a cause of sudden cardiac arrest, which occurs due to the development of either polymorphic ventricular tachycardia or ventricular fibrillation. For this reason, the proper diagnosis of the condition is of importance as is the management. The only proven therapy is an implantable cardioverter – defibrillator (ICD). Quinidine has been proposed as an alternative in settings where ICD's are unavailable or where they would be inappropriate.**

**Keywords:** *Brugada Syndrome, sudden cardiac death, arrhythmia, channelopathy, electrophysiology*

# A CONSISTENT APPROACH IN A PATIENT WITH COMBINED LIVER PATHOLOGY - A CASE REPORT

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## ABSTRACT

**Introduction: Hepatitis C is an infection, affecting millions of people worldwide. It causes liver injury, which may vary from minimal inflammatory changes through fibrosis and cirrhosis to hepatocellular carcinoma. Various causes such as autoimmune diseases and metabolic disorders can interfere, causing faster progression of fibrosis. In the era of Direct Active Antivirals (DAA) sustained virological response (SVR) is achieved in >90% of patients. The question is how could this improve hepatic function in patients with combined liver pathology.**

**Material and Methods: This case report describes a 34-year old woman with known compensated chronic liver disease caused by chronic hepatitis C, non-alcoholic steatohepatitis (NASH) and primary biliary cholangitis (PBC). The patient was assessed as partial responder to Ursodeoxycholic acid (UDCA) and late relapser to 12 week course of Sofosbuvir(SOF)/Ledipasvir and Ribavirin. The observation aimed to study the efficacy of a novel and strategic antiviral regimen and to follow the course of chronic liver disease with complex etiology.**

**Results: Considering physical, laboratory and ultrasound data, the patient was classified as Child-Pugh B liver cirrhosis (score 7). Positive sp-100 antibodies were found – a predictor for severe course of PBC. She had no history of clinical decompensation and on 24.12.2018 retreatment with SOF/Velpatasvir/Voxilaprevir was started for 12 weeks, part of compassionate use program, achieving a SVR24. Moreover, after HCV-eradication, the patient's parameters – albumin, prothrombin time, Child and MELD score were improved. Alkaline phosphatase and bilirubin levels remained elevated, which indicates a suboptimal response to UDCA, making the patient suitable for treatment with Obeticholic acid. Having anticholestatic and antifibrotic properties, this medication is considered to be beneficial not only for PBC, but also for NASH.**

**Conclusion: Patients with combined liver pathology remain a challenge. Seeking to influence the different factors is probably the key to improve liver function.**

**Keywords:** *combined liver pathology*

# AN EXOTIC CASE OF VIRAL MENINGITIS – TOSCANA VIRUS, MORE COMMON IN BULGARIA

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## ABSTRACT

**Introduction:** **Toscana virus (TOSV) is a phlebovirus transmitted to humans by Phlebotomus papatasi (arthropods). Its incubation period is from a few days to 3 weeks. Meningitis is a common manifestation of Toscana virus infection.**

**Materials and methods:** **The presented information is based on different scientific works published in reliable science and research websites: Centers for Disease Control and Prevention; PubMed; ScienceDirect. In one particular study conducted in Bulgaria 459 blood samples were tested for specific TOSV IgG Ab with ELISA kit. Participants were from 19 out of 28 districts in Bulgaria.**

**Results:** **The official morbidity from viral meningitis/meningoencephalitis in Bulgaria for the last 5 years shows an incidence peak in June – 82 cases, July – 102 and August – 125 (according to the National Center of Public Health and Analysis). Infection rates are highest in the summer when the sand fly is most active, making phleboviruses among the top causes of meningitis. In most cases, the diagnosis is only clinical and considered laboratory-confirmed if the bacterial results are negative. In the only study available for Bulgaria, 112 study subjects out of 459 individuals were tested positive for TOSV-specific IgG antibodies. This resulted in a total seropositivity of 24.4%. In addition, residency in the southern districts of Blagoevgrad, Kardzhali or Yambol and age over 60 years were established as risk factors.**

**Conclusion:** **Toscana virus is more widespread in Bulgaria than the western Nile virus, which gained popularity in recent years. As one of the three major causes for meningitis it needs to be studied especially now in this global world when people are travelling more and the risk of contracting TOSV increases significantly.**

**Keywords:** *Toscana virus*

# CASE OF ISCHEMIC STROKE IN A YOUNG ADULT WITH THROMBOPHILIA IN THE PRESENCE OF A PATENT FORAMEN OVALE

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## ABSTRACT

**Introduction: Stroke in young adults (age<55) is considered as being uncommon, 10-15% of all patients with stroke. Etiologic factors include patent foramen ovale (PFO), hypercoagulable states, dyslipidemia, tobacco smoking and hypertension. Several studies show that it is highly controversial whether these states are real causes or risk factors for stroke.**

**Methods and materials: A case of a 22-year old female patient with neurological deficiencies and no history of vascular or cardiac diseases is presented. CT-scan and MRI indicated left-sided cortical ischemic stroke in the region of gyrus postcentralis. For further examination the patient underwent transthoracic echocardiography, transcranial color Doppler sonography and transoesophageal echocardiography. Patent foramen ovale with significant right–to-left shunt was found on echocardiography. Genetic examinations showed mutations in the genes for Prothrombin and inhibitor of Plasminogen activator (PAI). Family history: the patient's father was diagnosed with submassive pulmonary embolism at the age of 52, deep venous thrombosis and proven thrombophilia (mutations in the genes for factor V, VIII, PAI and Prothrombin). The patient's sister, age of 28 is diagnosed with PFO with significant right –to- left shunt and proven thrombophilia (mutations in Prothrombin gene; mutation in PAI gene) and no history of vascular incidents. The patient's mother has no significant mutations in the genes for thrombophilia and has no history of vascular incidents.**

**Results: Percutaneus procedure was performed closing the atrial septal defect and the patient continued outpatient peroral treatment with anticoagulation medications.**

**Conclusion: Several studies show that main cause of stroke in young adults is thrombophilia and suggest PFO only to be a predisposing factor, increasing the risk of vascular incident. Other studies, on the other hand strongly suggest PFO to be a major cause of stroke in young adults. Young patients with stroke should be extensively observed for PFO and hypercoagulable states since they could be the major causes for embolic stroke of undetermined source.**

**Keywords:** *stroke, patent foramen ovale, thrombophilia*

# PERICARDIAL EFFUSION IN PREGNANCY – SCARY OR NOT?

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## ABSTRACT

**Introduction: There is no evidence that pregnancy affects susceptibility to pericardial disease and pregnant women do not show any specific predisposition to pericardial diseases. However, many pregnant women develop a minimal to moderate clinically silent hydropericardium, the most common form of pericardial involvement, usually as a benign mild effusion recorded in about 40% of pregnant women by the third trimester. Hydropericardium appears in late pregnancy (not before the 32nd week), is transient and generally well tolerated. Usually it can no longer be seen within 2 months after delivery of a normal child. The effusion is attributed to excessive water and salt retention in women with a higher mean weight gain at the late stage of gestation.**

**Materials and Methods: A 33-year old primigravida in 36 gestational week was admitted to Cardiology department because of dyspnea and palpitations. After the admission she underwent a transthoracic echocardiogram (TTE) that showed mild pericardial effusion. Blood tests were obtained. There was no evidence of an infectious or systemic autoimmune etiology of the effusion. She has gained more than 15 kg during the pregnancy.**

**Results: Pregnancy was continued with no anti-inflammatory or immunosuppressive medications until 38 weeks when a caesarean section was performed (following doctors' advice) and a healthy female child (3.2 kg, 47 cm, Apgar 8) was delivered. The pericardial effusion was still present after delivery and its size was reduced with no medications in one month.**

**Conclusion: During pregnancy the diagnostic approach is aimed at reducing useless investigations. Serial echocardiographies and blood tests to exclude other reason for effusion are needed to put the diagnosis hydropericardium. This is benign effusion that does not need further evaluation or medications and is not contraindication for normal labour.**

**Keywords:** *pericardial effusion, pregnancy, hydropericardium*

# GENTAMICIN-INDUCED ACUTE INTERSTITIAL NEPHRITIS

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## ABSTRACT

**Introduction: Acute interstitial nephritis (AIN) is defined as a renal injury characterized by inflammation and edema of the renal interstitium, usually resulting in abrupt decline of renal function. The classic triad of fever, rash and eosinophilia is uncommon. It is a possible complication of antibiotic treatment.**

**Materials and Methods: A 73-year-old male presented with malaise, chest pain, shortness of breath, fever up to 39°C and reduced urine output for the last couple of days. Prior to hospitalization, the patient was treated for 3 days with Gentamicin (x160mg/d/i.m.) for a respiratory infection. He presented with laboratory results: blood urea nitrogen (BUN) 28,5 mmol/l; Serum creatinine 459 mcmol/l; estimated glomerular filtration rate (eGFR) 11 ml/min, Uric acid 846 mcmol/l; C-reactive protein (CRP) 190,21 mg/l; Protein in the urine (2+); Urine sediment – erythrocituria, leukocyturia, bacteriuria. The patient started renal replacement therapy and four hemodialysis procedures were performed.**

**Results: As a result of hemodialysis treatment and intravenous administration of steroids urine output was recovered. The patient was discharged with laboratory results: BUN 16,8 mmol/l; Serum creatinine 219 mcmol/l; Uric acid 460; CRP 14,89 mg/l; eGFR 26 ml/min; Protein in urine (-); Uric sediment – 33 erythrocytes/ul. Close monitoring of urea, serum creatinine and urine after hospitalization was mandatory. Given the lack of evidence of previous renal disease, and the currently impaired renal function, AIN was considered as a reason for the acute kidney injury (AKI) because of the treatment with Gentamicin.**

**Conclusion: Acute interstitial nephritis is an uncommon but important cause of acute renal failure. Aminoglycoside antibiotics are still widely prescribed for the treatment of various infections. While concern of nephrotoxicity still exists, this adverse effect can be limited by utilizing these agents in the right population.**

**Keywords:** *Gentamicin-induced, interstitial nephritis*

# CASE REPORT OF A 5-MONTH-OLD INFANT WITH A NEUROBLASTOMA-ASSOCIATED PELIOSIS

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## ABSTRACT

**Introduction: Peliosis is a rare clinical diagnosis characterized by the presence of multiple blood-filled lacunar spaces in the liver. It is associated with infections, anabolic steroid administration and malignancies.**

**Materials and methods: A 5-month-old infant was admitted to the Second Pediatric Clinic in St. Marina Hospital - Varna after an outpatient examination and recommendation of a pediatric gastroenterologist. Complaints consisted of postprandial vomiting intensifying in the last month. The somatic status was carefully evaluated. Haematological, biochemical and microbiological parameters were dynamically monitored. The conflicting test results created differential diagnostic cases, refined through imaging and invasive studies. Abdominal ultrasound, tomography, and MRI were performed. Myelogram and flow cytometry of bone marrow, cranial scan and a subcutaneous biopsy were also assigned.**

**Results: The examination revealed a liver 2 cm below the rib arch with a round edge and a soft elastic consistency. Thick subcutaneous 0.5-1 cm formation was palpated under the navel - movable and not fused to the skin. Microbiological and bone marrow studies were negative. Ultrasound reviled multiple hypoechogenic lesions in both hepatic lobes with hyperechogenic halo. They were 7/8 mm in size, well-spaced and well-blooded. The lesions remained hypodense in the arterial phase and hyperdense in the late venous phase on CT scan. The MRI rejected the diagnosis of hemangiomas. In addition, a rounded formation with a hypointensive capsule was established in the upper pole of the left kidney. Pack of lymph nodes was found in the abdomen. Subcutaneous lesion biopsy referred to a neuroblastoma phenotype as evidenced by MLPA analysis - del (q11, q3). According to the findings and a medical literature search, liver formations were defined as peliosis.**

**Conclusion: In most cases peliosis is either accidentally detected or an autopsy finding. Therefore, it should be taken into account the differential diagnosis of atypical focal liver lesions.**

**Keywords:** *Peliosis, neuroblastoma, postprandial vomiting, focal liver lesions*

# CASE REPORT OF A 9-YEAR-OLD GIRL WITH A CROHN'S DISEASE ASSOCIATED TOXIC MEGACOLON

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## ABSTRACT

**Introduction: Toxic megacolon is a rare initial manifestation of Crohn's disease. It is a life-threatening condition that needs to be diagnosed and managed in a timely manner.**

**Materials and methods: A 9-year-old Polish girl was admitted to an Infectious Disease Hospital with a 4-day history of repeated vomiting of gastric and bile contents and bloody diarrhea. She was in a poor general condition, with abdominal pain and 38oC fever. In the course of diagnostic refinement and treatment she was transferred to the intensive care unit and the second pediatric clinic of St. Marina Hospital Varna. Many imaging studies were performed - ultrasound, radiography, CT and MRI of the abdomen. The worsening somatic status led to daily consultations with a pediatric surgeon and pediatric gastroenterologist. After the latest X-ray examination results, an expert medical collegium decided to perform an exploratory laparotomy. The intraoperative findings were histologically verified. Blood, biochemical, inflammatory and microbiological parameters were dynamically monitored.**

**Results: Laboratory findings showed inflammatory changes (leukocytosis with neutrophilia, increased CRP, low serum iron, etc.). Imaging studies sequentially demonstrated ascites, thickening of the colon and hydroaeric shadows, and finally a pneumoperitoneum. Under general anesthesia, a median laparotomy was performed and revealed a bloated large intestine with a bleeding contents. Its wall had decreased muscle tone with hemorrhagically infarcted areas. The pathological process involved the entire colon - 6-7 cm distal from the ileocecal valve to the rectum. Two perforations with a diameter of 8-10 mm were found. Toxic megacolon was diagnosed. The national pediatric surgery consultant suggested a total colectomy with ileostomy. The following morphological result proved the intraoperative diagnosis.**

**Conclusion: Dynamic and active monitoring of cases with toxic megacolon is a guarantee of lethality decrease. Immunosuppressive therapy due to guidelines successfully prevents the proximal intestinal tract inflammation and also the extraintestinal manifestations of Crohn's disease.**

**Keywords:** *Toxic megacolon, bloody diarrhea, median laparotomy, bloated large intestine, fulminant Crohn's disease*

# SEROPREVALENCE OF TOXOCARIASIS IN CHILDREN AND ADULTS OF NORTHEASTERN BULGARIA

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## ABSTRACT

**Introduction: Human toxocariasis is a helminthic zoonosis caused by larval stages of Toxocara canis and Toxocara cati. Contamination of the environment with helminth eggs from cats' and dog' feces is the key route of transmission. Humans contract the infection by ingesting embryonated eggs. There are four forms of the disease – covert, visceral larva migrans, ocular and neurotoxocariasis. The aim of this study is to establish the levels of seroprevalence of toxocariasis among children and adults in Northeastern Bulgaria.**

**Materials and Methods: Included in the current investigation is an actively selected group of 30 children and 51 adults with symptoms specific for the Toxocara infection (allergic reactions, rhinorrhea, ocular disturbances, cognitive disorders, epilepsy, iron-deficiency anemia, eosinophilia, ect.) and control group of randomly selected 61 healthy individuals. The seroprevalence of anti-Toxocara antibodies is determined by ELISA, followed by verification of the ELISA-positive findings with Western blot (WB).**

**Results: The preliminary ELISA tests showed 30 positive results and only 19 were confirmed with WB for the presence of specific anti-Toxocara antibodies. This results in an overall seroprevalence of 13.38% (19/142) in the investigated population. The rates demonstrated in children 10.00% (3/30) and adults 13.73% (7/51) with clinical symptoms corresponds with the increased environmental exposure over time. The highest result of 14.75% (9/61) in the group of healthy controls validates the mild and asymptomatic, hence "covert" course of toxocariasis, especially in adults.**

**Conclusion: ELISA essay is a suitable test for initial investigation of a large number of people but the observed cross-reactivity, demands verification of with more specific immunological methods like WB. The background seroprevalence of toxocariasis in Norteastern Bulgaria is significantly high and exceeds 10% in all the investigated groups. This demonstrates that the essentially unknown Toxocara-infection presents a considerable public health problem that requires further investigation and increased awareness.**

**Keywords:** *Toxocariasis, Toxocara infection, ELIZA, Western blot*

# REVIEW OF CASE STUDIES SHOWING DRUG-INDUCED HEPATOTOXICITY IN PATIENTS WITH VARENICLINE USE

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## ABSTRACT

**Introduction: Varenicline is an FDA approved prescription drug used for smoking cessation marketed as Chantix in the US and Champix in other countries. It works primarily by acting as a partial agonist of α4 β2 neuronal nicotinic acetylcholine receptors producing constant low levels of dopamine release in the reward centre leading to the reduction of nicotine withdrawal symptoms while diminishing the pleasurable sensation associated with smoking. The aim of this review is to find out information about the risk of hepatotoxicity with varenicline use.**

**Material and Methods: Case studies conducted from 2009 to 2018 showing various levels of hepatotoxicity in four patients aged 50-69 that have recently started Varenicline treatment were gathered and reviewed. The online databases PubMed, AASLD and SpringerLink were searched in order to collate the case studies and a pattern was observed among these patients.**

**Results: In all four case studies; patients developed liver damage 3-4 weeks after the start of varenicline administration. Laboratory testing showed increased aspartate aminotransferases, alanine aminotransferases, alkaline phosphate and bilirubin levels in all four subjects. Other common symptoms included nausea, vomiting, jaundice and pruritus. Following discontinuation of Varenicline, the hepatic biomarkers returned to normal levels within 4-10 weeks indicating the cause of the liver damage as drug induced.**

**Conclusion: Varenicline has been proven to be effective in smoking cessation and the benefits are likely greater than the risks posed. However, as indicated by the patients above severe hepatotoxicity can follow in some cases which can lead to acute liver failure along with a string of comorbidities and ultimately death if not managed appropriately. Therefore, physicians should be made aware of the hepatotoxicity that could potentially occur in order to make an informed decision when prescribing the medication.**

**Keywords:** *Varenicline; hepatotoxicity*

# CLINICAL MANIFESTATIONS OF A PATIENT PRESENTING WITH STAGE 3 PARKINSON'S DISEASE AND TREATMENT WITH DOPAMINE PRECURSOR L-DOPA

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## ABSTRACT

**Introduction:** **Parkinson's disease (PD) is a common neurological disorder mainly affecting individuals over the age of 60. It is a progressive disease characterized by stages 1- 5 with symptoms emerging slowly over weeks and months. There is no laboratory testing or imaging study required for confirming diagnosis of parkinsonism, however all sufferers display 3 cardinal symptoms; autonomic dysfunction, bradykinesia and impaired balance. The most common complaint on initial admission to the hospital is a resting tremor.**

**Materials and methods:** **A 68-year-old woman was admitted with a knee injury from a fall due to a loss of balance. On physical examination, she displays slow eyeblinks, reduced hand gestures and spontaneous movement, expressionless face (hypomimia) and a mild tremor; all hallmarks of stage 3 Parkinsonism. Historically, she was able to perform daily household tasks but now experiences difficulties completing activities such as dressing and washing.**

**Results:** **Neuropathologic findings of the disease involves the loss of dopaminergic neurons from the pars compacta of the substantia nigra in the brain. As the number of dopamine receptors decline, physical manifestations in the form of tremors and bradykinesia in one or more limbs occurs during the earlier stages. Patients undergo oral therapy with L-dopa, a precursor of dopamine which restores some fine motor control. The presence of fibrillar aggregates called Lewy bodies (LBs) can be found in 10% of the pigmented neurons in the substantia nigra.**

**Conclusion:** **The exact cause of idiopathic Parkinson's disease is unknown, and affects every patient differently, with varying clinical symptoms presented. Levodopa therapy has shown to play a role in management of Lewy body count, and research is ongoing to establish the correlation between their number and REM sleep disorders prevalent in PD sufferers. At dosages of 1200 mg/d, responses to Levodopa are virtually non-existent.**

**Keywords:** *Neurology, Alzheimer's, Lew bodies (LBs), REM sleep disorders*

# BENTALL PROCEDURE

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## ABSTRACT

**Introduction: The Bentall procedure is considered the gold standard in the treatment of patients requiring aorticroot replacement. It is a type of cardiac surgery involving composite graft replacement of the aortic valve, aortic root and ascending aorta with re-implantation of the coronary arteries into the graft. This operation is used to treat combined disease of the aortic valve and ascending aorta.**

**Materials and Methods: The case refers to a 69-year-old man who consulted his doctor because of dyspnea and fatigue.The anamnesis showed that the patient has a risk profile of coronary heart disease – sex, age, bad habits – smoking and drinking alcohol, high blood pressure and family burden of heart failure.**

**Results: The physical examination revealed a crescendo diastolic sound, which was best heard over the second intercostal space at the right sternal border. After anX-Ray was performed, the patient was diagnosed with aneurysm of the descending aorta under a. subclavia sinistra, aortic root and high-grade aortic insufficiency. The results were confirmed by CT scanand aortography. Because of the risk of distal embolization, the cardiac surgeons and invasive cardiologists decided to first implant the stent-graft into the descending aorta and afterwards for the aortic root prosthetic and change of the aortic valve.The stent- graft was implanted in descending aorta, using the left femoral artery and a month later – BioBentall procedure was performed and the patient's condition was improved.**

**Conclusion: While very complex and requiring excellent work from both – cardiac surgeons and invasive cardiologists, this case shows the importance of cross-field collaboration and the success it brings, concerning patient health.**

**Keywords:** *Bentall procedure*

# MORPHOLOGY AND MECHANISMS OF EVOLUTION OF FRANK'S SIGN

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## ABSTRACT

**Introduction: Frank's sign is a diagonal crease of the ear lobe, supposedly related to cardiac pathology and has strongly been associated with coronary artery atherosclerosis. Although described in the 1970s, Frank's sign can be traced back through art to ancient Rome and emperor Hadrian, wo was commonly depicted as having Frank's sign on statues and his death was chronicled as being attributed to acute myocardial infarction.**

**Materials and Methods: A total of 45 consecutive adult patients referred for autopsy in a one-and-a-half-year period were extensively studied. Samples from both the ear lobes were obtained for histopathology, as well as cardiac samples from all four cardiac compartments. The patient data and cardiac parameters were statistically analyzed with MaxStat Pro, with a two-tailed t-test $p<0.05$ considered statistically significant.**

**Results: When compared patient with Frank's sing and those without it had no statistical difference in age (P=0.0575). There was however a statistically significant increased cardiac weight (P=0.0005), left ventricular wall thickness (P=0.0002) and right ventricular wall thickness (P=0.0043). Histopathology obtained from the ear lobes revealed myoelastofibrosis in an arterial vessel, located at the base of the crease and diffuse fibrosis with Wallerian-like degeneration - eosinophilic inclusions in the peripheral nerves. These changes suggest a time-related progression of the crease-associated changes due to chronic hypoxia and reoxygenation injury on the background of the embryological development of the auricle and it physiologically lower oxygen saturation.**

**Conclusion: Our data suggest a significant correlation between the morphological changes of the myocardium and the presence of the ear lobe creases, with arterial myoelastofibrosis, Wallerian-like degeneration in peripheral nerves and deep tissue fibrosis found in the base of the crease.**

**Keywords:** *Frank's sign, ENT, myoelastofibrosis, ear lobe*

# MYXOMA - A CASE REPORT

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## ABSTRACT

**Introduction: Myxoma is a very rare primary cardiac tumor. At the same time, it is the most widespread of that tumor type. The general occurrence of the benign tumor is in the left atrium (LA) and it grows on the atrial septum. Myxomas are more frequent in women.**

**Materials and methods: This report is about a 43-year-old patient, with complaints of about a year of shortness of breath, mild fatigue, loss of appetite and about a month with fever up to 38°C. Regarding these complaints, she was hospitalized and treated for Pneumonia. Due to persistence of complaints she was directed for hospitalization in University Hospital. There are no co-morbidities. The chest X-ray reveals cardiomegaly, pulmonary congestion and a small pleural effusion. The performed Computed Tomography of the chest and abdomen shows pleural effusions, ascites, stagnant lungs and LA filling defect. Electrocardiography - sinus rhythm, incomplete right bundle branch block. Echocardiographic (ECHO) examination shows a large tumor formation in the left atrium, passing through the valve orifice with significant obturation and II degree mitral and tricuspid regurgitation. Transoesophageal ECHO confirms the diagnosis. The patient was operated after consulting with a cardiac surgeon.**

**Results: The operation was performed under conditions of extracorporeal circulation. The tumor formation from the LA was extirpated. An anuloplasty of the tricuspid valve was made. Patient recovery was monitored for possible complications and relapses after the surgery. Biopsy of cardiac muscle with sub endocardial fibrosis, shows a morphological pattern corresponding to LA Myxoma.**

**Conclusion: Myxoma shares common symptoms with other diseases, making it difficult to diagnose. It is usually an incidental observation during routine ECHO. Failure to detect it in time can result in death.**

**Keywords:** *myxoma, tumor, left atrium*

# MANIFESTATION OF HUNTINGTON'S DISEASE - CASE REPORT

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## ABSTRACT

**Introduction: Huntington's disease in a hereditary progressive brain disorder, characterized with hyperkinesis and intellectual degradation. It affects 5-10 per 100 000 people and the main age of onset is 35-40 with an average lifespan of 15-20 years. The disease is caused by an autosomal dominant mutation in CAG triplet series in the huntingtin gene (HTT) on chromosome 4, which results in a protein with an abnormally long sequence. The diagnosis of Huntington's disease is generally confirmed by the patient's family medical history and through a genetic test for the presence of the expanded HTT gene.**

**Materials and Methods: The case report describes a 59-year old man who presented with increasing involuntary movements of the left leg, shoulder and abdomen. The symptoms had become more frequent with time, affecting the four limbs, head and respiratory muscles. The manifestation included also psychiatric changes like aggravation and memory loss. The symptoms are present only at rest and disappear while sleeping. The patient's father is known to have similar symptoms for which he never sought medical help.**

**Results: The results from the CT showed dilatation of the lateral ventricles, intercaudate distance – 21.55 mm and ration to the inner table – 1.85 which are signs of caudate nucleus atrophy. The psychology consultation results showed reduced personal, cognitive levels and decreased intellectual activity – IQ 61. Considering these results, patient's clinical profile and family history a genetic disorder was discussed. The gene testing is in the process and therapy with Haloperidol was started and improvement was reported.**

**Conclusion: Huntington's disease is an autosomal dominant disorder that has 50% chance to be inherited. There is no cure for Huntington's disease but there are approved symptomatic therapies. Early diagnosis can lead to preventing the neurodegenerative process. This will slow the progression, prolong overall functioning and improve patient's quality of life.**

**Keywords:** *Huntington, chorea, neurodegenerative, hereditary, hyperkinesis, huntingtin*

# PARENCHYMAL ORGAN CHANGES ASSOCIATED WITH CORNELIA DE LANGE SYNDROME – A REPORT OF TWO AUTOPSY CASES

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## ABSTRACT

**Introduction:** **Cornelia de Lange (CdLS) is rare genetic disorder with polyfactor etiology. The syndrome features a wide variety of physical and cognitive hallmarks such as distinctive facial appearance, small stature, bone and gastrointestinal abnormalities.**

**Material and methods:** **Two cases of patients clinically diagnosed with CdLS are reported. Both cases were diagnosed and treated at the St. Marina University Hospital, Varna, Bulgaria and were referred for autopsy after death. The first case was of a female patient, aged 7 and the second of a 17-years-old female. Both patients had family history, severe features and complications associated with CdLS.**

**Results:** **In both cases, the liver had normal anatomical proportion with a slightly flattened shape especially pronounced in the second case where, the liver had a pyramidal shape with sharp edges. The kidneys in both patients were with a flattened pyramidal shape, with the tip located at the hilum and a base toward the lateral abdominal side. Both patients also had a pyramidal shaped spleen, again with the tip located at the hilum, with the second patient having multiple accessory spleens along the splenic artery. Cause of death in both patients was determined as complications from CdLS.**

**Conclusion:** **Pyramidal form of the parenchymal organs is a manifestation that has so far not been described in CdLS patients. Despite atrophic organs sometimes having the same appearance, different organs are rarely affected identically, hence these changes can be considered as specific features of CdLS.**

**Keywords:** *Cornelia de lange, morphology, parenchymal changes, genetic disorders*

# LATE ENDOCRINE PANCREAS PATHOMORPHOLOGIC FEATURES IN PATIENTS WITH TYPE 2 DIABETES

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## ABSTRACT

**Introduction: Islet amyloid polypeptide (IAPP) amyloidosis is a pathologic alteration of the pancreas, represented by abnormal accumulation of amylin in the interstitial tissue. Amylin is a neuroendocrine hormone, co-secreted with insulin by b-cells and participating in downstream regulation of postprandial glycaemia. The aim of this report is to examine IAPP amyloidosis as a late consequence of poor control of blood glucose levels in patients with type 2 diabetes (T2D) who have been referred for autopsy.**

**Materials and methods: A total of 34 consecutive autopsies performed at the St. Marina University Hospital, Varna, Bulgaria, carried out by a single pathologist were included into the study. Samples from the tail of the pancreas were obtained to evaluate the state of the changes and were analyzed together with the specific organ changes associated with T2D, as well as the medical documentation of the patients.**

**Results: Of the 34 autopsies, 10 cases (six female and four male) were included in the study, seven of whom had medical history of T2D. The average age was 65,7 years (ranging from 50 to 85 years). In all of the cases morphological features of fibrosis and lipomatosis were present, with one of the patients having signs of pancreatic amyloidosis- Congo red positive deposition of pink, amorphous material in the extracellular matrix.**

**Conclusion: The described pathological alterations in all of the cases illustrate the progressing impairment of the structure of the pancreas, especially b-cells dysfunction in late stages of T2D and highlight IAPP amyloidosis as the cause of irreversible damage of the isles of Langerhans and b-cell death.**

**Keywords:** *pancreas; diabetes; amyloidosis*

# WOAKES' SYNDROME: A CASE REPORT

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## ABSTRACT

**Introduction: Woakes' syndrome is a rare condition of nasal pyramid deformity, caused by massive polyp growth in the nasal cavity and paranasal sinuses. The etiological reason causing the chronic hyperplastic sinusitis and nasal polyposis remains undetermined. Recently, both allergy and a non-allergic inflammation such as primary ciliary dyskinesia of the polyps have been discussed as a possible underlying cause of the syndrome.**

**Case report: A 55-year-old female patient had first reported to the ENT Department of the University Hospital St. Marina in Varna, Bulgaria, in 2019, with progressive nasal obstruction. Symptoms had begun 10 years prior to the examination but had been left untreated. She presented with progressive face asymmetry with broadening of the nose.**

**Results: The physical examination revealed a woman in good health with complete bilateral nasal blockage due to polyps, which were observed in both nares and a progressive widening of the bony and cartilaginous nose. The patient reported a recurrence of nasal obstruction with a loss of sensitivity for smell and an increasingly notable nasal deformity in the last 3-4 years. Anterior rhinoscopy showed extensive nasal polyps obstructing all of the cavum and the entire vestibulum nasi on both sides. CT scan revealed a complete obliteration of the paranasal sinuses on both sides with a protruding of the ethmoid walls into the orbits. In order to restore the air passage an endonasal endoscopic polypectomy and ethmoidectomy were performed.**

**Conclusion: The etiology of Woakes' syndrome remains undefined. Systemic treatment and topical anti-allergy medications should be undetaken to prevent the redevelopment of the nasal polyps.**

**Keywords:** *Woakes' syndrome*

# SURGICAL PATHOLOGY AND ORTHOPAEDICS

SURGICAL PATHOLOGY AND ORTHOPAEDICS

# CURRENT DIAGNOSTIC APPROACHES TO HEPATIC ENCEPHALOPATHY

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## ABSTRACT

**Introduction: Hepatic encephalopathy (HE) is a severe complication in patients with liver cirrhosis that affects more than 40% of them. It is also observed in patients with portal hypertension due to other reasons such as hepatic vein thrombosis and idiopathic non-cirrhotic portal hypertension. The condition is divided into covert and overt HE. The latter presents with disorientation, intellectual impairment and tremors (asterixis) among other symptoms and usually leads to hepatic coma, if left untreated. Currently, diagnostic approaches vary considerably among different guidelines.**

**Materials and Methods: The research is based on information from the platforms PubMed and AWMF using the following keywords: covert and overt hepatic encephalopathy, diagnosis, tests, Diagnostik, hepatische Enzephalopatie. The articles reviewed have been published between 2014 and 2018.**

**Results: Defining the grade of overt HE is done by using the West Haven Criteria (WHC) or by examination of impaired neuromotor function. Diagnosis of covert HE, on the other hand, is still a challenge due to the lack of apparent symptoms and the risk of subjective findings. It may be reached by using one or a combination of tests, divided into three main groups – paper and pencil tests, computerized and neurophysiological tests. Of these, the last group, which includes electroencephalography (EEG) and critical flicker frequency (CFF), is the most reliable and detects early signs of covert HE.**

**Conclusion: Since covert HE is a condition that could affect the patient's quality of life, it is essential for a diagnosis to be established as early as possible. Furthermore, diagnosing it is the first step towards appropriate treatment, which could prevent complications and extend the life expectancy. However, even the most sensitive tests are either too time-consuming or require expensive equipment. More research is needed to create a diagnostic approach that can be fully effective and applied worldwide.**

**Keywords:** *hepatic, encephalopathy, diagnostic, approach*

# RARE CASE OF AGGRESSIVE PAPILLARY THYROID CARCINOMA

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## ABSTRACT

**Introduction: Papillary thyroid carcinoma (PTC) is considered the least malignant of the thyroid gland cancers. In recent years the incidence of all thyroid neoplasms has risen. Most papillary carcinomas are identified in early stages and due to their relatively slow growth process the prognosis is highly satisfying. Nevertheless, in advanced cases the usual treatment may not show definitive results which implies close observation of the neoplasm and alteration of the therapy.**

**Materials and methods: A 66 years old female is hospitalized in the endocrinology department for a follow-up (after initial treatment for PTC). In 2018 a total thyroidectomy with neck lymph node dissection was performed followed by a postoperative radioiodine treatment with 130 mCi of 131I. The reason for the operation was papillary thyroid carcinoma, classical variant with lymph node metastases (T4aN1bMxG1).**

**Results: A full blood panel was done. Our attention was caught by the increased thyroid-stimulating hormone (TSH) – 9.526 mIU/L, indicating insufficient thyroxin replacement as well as thyroglobulin level of 2.98 ng/mL. Echography of the neck was performed. In the thyroid bed there was no thyroid parenchyma. In front-right of the thyroid bed a parenchymal formation with dimensions 9.1/5.5 mm was found, laterally a similar formation was visualized (5/5 mm). Bigger lesion was encountered on the front-left of the trachea (10/7.3 mm). Differential diagnosis includes local relapse of the cancer or bigger lymph nodes. A conclusion that the patient is eligible for a second radioiodine therapy was reached. Concerning the hypothyroidism, a change in the L-thyrox dosage was suggested.**

**Conclusion: Papillary thyroid carcinoma is easily treated when diagnosed in time. However, in rare and undiagnosed cases it can spread to the surrounding tissue and muscles. In those cases, one round of radioiodine could not be enough and relapses could occur.**

**Keywords:** *papillary thyroid carcinoma, aggressive, TSH*

# NECROTIZING SKIN AND SOFT TISSUE BACTERIAL INFECTION IN A TYPE 2 DIABETIC PATIENT – A CASE REPORT

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## ABSTRACT

**Introduction:** **Necrotizing soft tissue infections (NSTIs) are a large group of infections including cellulitis, fasciitis and myositis. They can be classified as monomicrobial or polymicrobial, depending on the different type of bacterial species present. NSTIs are defined as a diffuse inflammatory process that involves the subcutaneous fat, neurovascular structures, and fascia, leading to significant tissue destruction, presented with gross suppuration. Patients should be treated with infusion of fluids, broad spectrum antibiotics and surgical debridement.**

**Materials and Methods:** **A 55-year-old female patient was admitted in the Second Department of Surgery with a clinical presentation of a NSTI of the lower abdomen extending to the left femoral and inguinal regions. Upon physical examination she was unresponsive, with high fever. The last few days the patient was feeling unwell and had multiple episodes of nausea and vomiting. Skin findings revealed substantial tissue necrosis affecting the abdominal wall, with greyish discoloration and pus drainage. Microbiological testing was conducted and there was an evidence of a polymicrobial infection (P. aeruginosa and P. mirabilis) both sensitive to meropenem and metronidazole. Laboratory results showed the presence of hypoglycemia and impaired kidney function, the patient has a history of type 2 diabetes.**

**Results:** **Aggressive surgical debridement including fasciotomy and necrectomy were performed followed by pressure irrigation of the wounds with sterile saline and antiseptics. The mentioned procedures were repeated several times over, during the patient's stay. Three weeks later, she was discharged from the hospital.**

**Conclusion:** **Unusual and rapidly progressive, such disease can present as a form of superficial abscess or cellulitis. High morbidity and mortality rates suggest a more serious condition. Glycemic control should be taken in consideration to optimize appropriate wound healing and to minimize the risk of infection in patients with diabetes.**

**Keywords:** *surgery, abdomen, septic, diabetes, fasciitis*

# A CASE REPORT OF A METASTATIC OSTEOCLASTOMA

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## ABSTRACT

**Introduction:** **Osteoclastoma is a rare tumor of the bone. It is presented by multinucleated giant cells, which are normally benign. Malignancy in giant-cell tumor occurs in about 2% of all cases with chance for distant metastases, mainly in the lungs.**

**Materials and methods:** **A 32-year-old male patient presented on 08.2019 with complains of aggravated pain in the right thigh with a duration of 20 days. On a physical exam there was a painful formation in the middle third of the patient's right thigh. His medical history showed a surgery performed in 2018 in Germany of an aneurismal cyst with benign characteristics in the diaphysis of the right femur.**

**Results:** **The following investigations were performed: a PET-scan showed a heterodense tumor formation with zones of hypo- and hyper metabolism of SUV-max 13 in the femur and the thigh musculature; in the lower lobs of the lungs several nodular lesions with the size of 3mm were detected; a single osteosclerotic nodule was reported in the right scapula with a diameter of 5mm. The biopsy showed a tumor of osteoclast alike giant cells and mesenchymal cells with significant number of cystic spaces filled with blood and surrounded by osteoclasts and granulation tissue. The tumor cells and the multinucleated cells had a nuclear atypism. Immunohistochemical staining with p53 showed focal positivity and Ki-67 ~15% (>10% is considered high proliferative index).**

**Conclusion:** **There is no universally recognized treatment modality for metastatic osteoclastoma (MO). Regardless of the histological picture, there is a need of an established standard for diagnosis, follow-up and treatment of patients with such a tumor due to its unusual behaviour. Current strategy for the treatment of MO includes surgical excision and biological course of Denosumab, which has a promising activity in osteoclastoma treatment, including pulmonary metastasis.**

**Keywords:** *Osteoclastoma, bone tumor, giant cells tumor, metastatic osteoclastoma*

# VERTEBRAL COLUMN SHAVER'S DISEASE WITH SPINAL CORD COMPRESSION, MIMICKING POTT'S DISEASE - CASE REPORT

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## ABSTRACT

**Introduction: Shaver's disease of the lung and pleura is a very rare disease, which is mainly seen at aluminium powder workers. Nowadays such a disease is considered an almost forgotten one. Numerous publications about lung aluminosis were found, but in none of them vertebral column aluminosis was mentioned. Methods and materials: A 59-year-old man was admitted to "St. Anna" Hospital, Varna with girdle pain in the lower thoracic half. The patient underwent explorative thoracotomy due to posterior mediastinum tumor formation. The biopsy showed Nodular form of pneumoconiosis. After a month the patient was hospitalized due to lower paraparesis with diminished reflexes, conductive type of sensory deficit at the level of dermatomes Th5-6 and urinary retention. He stated that in the 1970s he worked as polisher and has been exposed to non-greased aluminium powder for 3-4 years.**

**Results: X-ray of thorax revealed a V-shaped shadow and contrast-enhanced signs for paravertebral cold abscess with discitis. The sputum smear showed no growth of mycobacteria, although MANTOUX test was positive. A laminectomy of Th5 was performed and a dark black lobulated tumor formation was found entering the vertebral canal in an hourglass shape. The first biopsy result was metastatic melanoma. Considering the patient exposure different tools for diagnosing aluminosis were used such as T-cell lymphocytosis test in bronchoalveolar lavage fluid, in-vitro blastogenic response of peripheral blood lymphocytes to soluble aluminium compounds, electron microscopy. In the absence of these specialized tests the Irwin's aluminium stain is a helpful alternate diagnostic tool.**

**Conclusion: Aluminosis can mimic tuberculosis and histopathologically metastatic melanoma or pneumoconiosis. Therefore, it's important to have a wide spectrum of differential diagnosis when first evaluating a patient and put special emphasis on history and occupational exposure.**

**Keywords:** *Shaver's disease, Aluminosis, Vertebral column, Irwin's stain*

# APPLICATION OF SELF-EXPANDABLE METALLIC STENTS IN ESOPHAGEAL DISEASES

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## ABSTRACT

**Introduction: Benign and malignant diseases of the esophagus can cause either obstruction or perforation as part of their natural development. Postoperative anastomotic leaks are another devastating consequence of esophageal surgery. Iatrogenic perforations due to instrumental examinations is another vast group of esophageal pathologies requiring difficult decision making. Management is associated with extensive surgery or minimally invasive placement of self-expandable metallic stents (SEMS) facilitating short recovery time and better quality of life for patients.**

**Materials and methods: Retrospective study was performed in the period 2014-2019 of 27 patients with placement of SEMS. Indications included malignant obstruction, perforation and trachea-esophageal fistula. The location of stenosis was verified with esophagoscopy, malignant processes were histologically verified. The upper position of the stent was marked by injection of intramural contrast with endoscopic injector and the stent was placed under fluoroscopic guidance. Control plain X-ray was performed after 24 hours. Enteral feeding was restored after 24 hours and control plain X-ray.**

**Results: The most frequent causes for SEMS application was nonresectable esophageal cancer (63%, n= 17), external compression caused by lung carcinoma (14.8%, n=4), spontaneous esophageal perforation (7.4%, n=2) tracheoesophageal fistulas caused by lung carcinoma (7.4%, n=2), iatrogenic perforation (7.4%, n=2). Median body mass index (BMI) of patients was less than 18.5. Severe stages of malnourishment were recorded. No complications related to the procedure were recorded. Recurrent dysphagia was noticed in n=3 patients. Migration of the stent was established in n=1 patient with esophageal carcinoma, and in 1 spontaneous perforation. Pre-stent stenosis n=1. Stent ingrowth n=2 in esophageal carcinoma, trachea-esophageal fistula n=1, bleeding n=1 with esophageal carcinoma.**

**Conclusions: Minimally invasive SEMS placement for palliative treatment of malignant obstructing pathologies facilitates less trauma and hospital stay while patients reserve their ability for enteral feeding. Management of postoperative leaks, malignant fistulas or iatrogenic perforations allows to salvage patient's esophagus.**

**Keywords:** *esophagus, stenosis, rupture, perforation, fistula, minimally invasive, stent placement*

# CONGENITAL CHOLESTEATOMA OF THE MASTOID CAVITY

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## ABSTRACT

**Introduction: Cholesteatoma is a well-demarcated, non-neoplastic lesion in the temporal bone. It is composed of desquamated keratinizing stratified squamous epithelium forming a mass. Their cholesterol content is responsible for the name cholesteatoma. Keratoma and epidermoid cyst are more appropriate names suggested to describe the same condition.**

**Materials and methods: We present a 70-year-old female patient with pain in the right ear and severe headaches with vertigo for the past four months. She also reports a foul-smelling discharge from the same ear. On examination the patient had a fistula on the posterior surface of the external auditory canal communicating with the mastoid cavity. Computed tomography and magnetic resonance imaging were performed. They showed a heterogeneous osteolytic lesion in the right temporal bone measuring 48x50x13 millimeters. The lesion involved the mastoid cavity and extended to the base of the posterior cranial fossa without intracranial extension. Another bone erosion was seen in the apex of the pyramid measuring 22x12x14 millimeters. Obliteration of the right sigmoid sinus was suspected.**

**Results: After general anesthesia radical mastoidectomy was performed. The lesion was removed under microscope guidance and sent for histopathological examination. The external auditory canal was reconstructed, and the fistula was resected. The pathology report confirmed the diagnosis of cholesteatoma. The patient underwent broad-spectrum intravenous antibiotic therapy. After an uneventful postoperative period, the patient was discharged home on the eighth postoperative day in good general condition.**

**Conclusion: Congenital cholesteatoma of the mastoid cavity is a rare disease with an often-delayed diagnosis. Despite being benign, when not diagnosed timely, it can progress with invasion and bone destruction and lead to complications.**

**Keywords:** *cholesteatoma; keratoma; mastoidectomy*

# MINIMALLY INVASIVE DIRECT CORONARY ARTERY BYPASS - A KEYHOLE HEART SURGERY

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## ABSTRACT

**Introduction: Minimally Invasive Direct Coronary Artery Bypass (MIDCAB) is a surgical treatment for coronary heart disease that gains surgical access to the heart through a smaller, intercostal incision in contrast to the classical medial sternotomy access. MIDCAB is suitable, less invasive method for coronary artery revascularization in single-vessel coronary artery disease.**

**Materials and methods: A case report of a 65-year-old man with single vessel coronary artery disease with medical history of Percutaneous Coronary Intervention (PCI) on Left Anterior Descending Coronary Artery (LAD), angina pectoris class III NYHA, hypertension class III, dyslipidemia, who was admitted in the Department of Cardiac Surgery, complaining of chest pain, breathlesness and fatigue during physical effort. After the coronary angiography single-vessel coronary artery disease was diagnosed with 70% proximal and 70% in stent restenosis on LAD. He was considered as suitable for MIDCAB surgery in planned order.**

**Results: The blood flow in the LAD has been restored with Left Internal Mammary Artery (LIMA-to-LAD graft) and the result was measured by flowmetry in the operation theater. After the operation, the patient was transferred to Intensive care unit, haemodynamically stable without significant rhythm and conduction disorders. No signs of respiratory insufficiency were observed after the extubation.**

**Conclusions: Overall MIDCAB revascularization as a very valuable concept within the different options of surgical heart revascularization. By avoidance of medial sternotomy and heart-lung machine it represents an effective way of revascularization of the LAD with arterial graft. The procedure is associated with a low level of complications peri- and postoperatively, also with high graft patency rates in the mid-term and long-term course.**

**Keywords:** *MIDCAB, Cardiac surgery, revascularization, surgery, coronary artery disease, bypass, minimally invasive*

# APPLICATION OF SURGICAL CRYOABLATION IN THE TREATMENT OF LEFT VENTRICULAR ANEURYSM

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## ABSTRACT

**Introduction: The intraoperative use of cryoablation in cardiac surgery is mainly applied to treat a wide set of arrhythmias (atrial fibrillation, AV node reentrant tachycardia, ventricular tachycardia etc.), by targeting the substrate directly. The main advantages of the procedure are reduced risk of damage to the surrounding tissues, better stability of the probe, and increased energy output.**

**Materials and Methods: A 63-year-old woman was admitted with sustained ventricular tachycardia and episodes of syncope. Previously the patient had been diagnosed with a left ventricular aneurysm and Hypertrophic Obstructive Cardiomyopathy (HOCMP). For the latter two septal alcohol ablation procedures were done. Preoperative ECG, 24-hour Holter monitoring, cardiac ultrasound and selective coronary angiography were performed. The ejection fraction was 21%. The left anterior descending artery had a stenosis of 40%. The recurrent episodes of ventricular tachycardia prompted the need for an urgent intervention. Before establishing cardiopulmonary bypass (CPB), three more episodes of ventricular tachycardia required external electrocardioversion.**

**Results: As a solution circular cryoablation was utilized, together with endoaneurysmal circular patch plasty repair in order to block re-entry pathways and restore the shape of the left ventricle. After the patient was weaned from CPB, no more episodes of arrhythmia were registered. The patient was discharged with stable sinus rhythm and increased ejection fraction (40%).**

**Conclusion: Surgical cryoablation is a comparatively easy, cost – effective and time – reducing technique with good results for handling arrhythmias in patients refractory to other medical treatments. It is safe and effective to be used in concomitance with other cardiac surgery procedures.**

**Keywords:** *Cardiac Surgery, cryoablation, surgery, ventricular tachycardia, ventricular aneurysm*

# SHORT AND LONG-TERM RESULTS AFTER LAPAROSCOPIC ADJUSTABLE GASTRIC BANDING (LAGB) SURGERY

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## ABSTRACT

**Introduction: It is well known that laparoscopic adjustable gastric banding (LAGB) is effective for weight reduction in severely obese patients. However, the data about its effect on further health state are poor.**

**Materials and Methods: This study included moderately (with present health issues) and morbidly obese patients, ≥18 years of age, who underwent LAGB surgery at Vilnius University Hospital between October 2009 and October 2019 and were eligible for this retrospective study. All the patients were identified through the hospital's electronic data system. Demographics, weights at baseline and follow-up visits (up to 10 years following surgery), and post-operative complications were documented. Follow-up visits occurred at unevenly spaced intervals within patients.**

**Results: This study included 97 (out of 208) patients (68 % female and 32% male, mean age 37 years, mean baseline BMI 46,9 kg/m$^2$). Complications developed in 9 patients (9,27 %), the most frequent being prolapse (25 %), access port problems (7 %), and explantation (1.2 %). 6 of 9 patients underwent reimplantation of LAGB surgery and it was successful. Anthropometric and cardio-metabolic variables were measured at baseline, 1 year, 5 years and 10 years after LAGB. Fasting glucose and insulin levels, triglycerides, AST, and ALT were significantly reduced, and HDL cholesterol significantly increased, which reduced the risk of cardiovascular and other diseases.**

**Conclusions: Obesity has constantly been associated with cardio-metabolic abnormalities, including dyglycemia, insulin resistance, hypertension, dyslipidemia, which may increase the risk of cardiovascular diseases and type 2 diabetes. The study has shown that complications after LAGB surgery has no major impact on human health, but significant metabolic changes definitely prolong survival of patients' life.**

**Keywords:** *Laparoscopic adjustable gastric banding, complications, metabolic changes, weight loss*

# IATROGENIC AORTIC DISSECTION: CLINICAL CASE REPORT

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## ABSTRACT

**Introduction:** **Aortic dissection, a rare complication of percutaneous coronary intervention, that can be fatal when it is not recognized and treated promptly. Treatment varies from conservative management to invasive aortic repair and revascularization.**

**Materials and Methods:** **A 54-year-old woman was complaining of chest pain, fatigue, shortness of breath occurring after moderate physical exertion. Patient had several risk factors of coronary artery disease: dyslipidemia, family history of premature cardiovascular disease, physical inactivity, obesity, a history of arterial hypertension for more than 20 years and diabetes mellitus (type II) for more than 10 years. During cardiac ultrasound possible hypokinesis of anterior and lateral walls and diastolic dysfunction (pseudonormal type) with normal left ventricular ejection fraction were observed. Cardiac stress test veloergometry was interrupted due to hypertension reaction to physical activity (submaximum heart rate was not reached). Others imagining tests were not performed. The patient was directed to the University hospital for the coronary angiography procedure. Theblood test results were in normal ranges and ECG showed no significant changes.**

**Results:** **During right coronary artery angiography, extensive right coronary artery dissection from the ostium to the ascending aorta occurred. The procedure was switched to the right coronary artery stenting to enclose the dissection gates and it was not successful. The urgent consultation of intensive care doctors, cardiosurgeons and interventional cardiologists decided to perform chest computed tomography angiography (aortography) and perform urgent surgery to treat dissection. During the surgery ascending aortic prosthetic reconstruction and aortocoronary bypass were performed forming distal vein junction to posterior interventricular right coronary artery branch.**

**Conclusion:** **Diagnostic coronary angiography is a frequent procedure with very low risk, especially when done in an optional situation (<1.3%). Moreover, diagnostic coronary angiography should only be performed with very strict and accurate indications, after proving non-invasive ischemia.**

**Keywords:** *Aortic dissection, iatrogenic, coronary angiography, coronary disease*

# CHRONIC CHOLECYSTITIS DUE TO EXACERBATED CALCULOSIS IN MICROSPHEROCYTIC ANEMIA OF MINKOWSKI- CHAUFFARD - CASE REPORT

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## ABSTRACT

**Introduction: Microspherocytic anemia of Minkowski- Chauffard is a hereditary disease that presents with abnormal red blood cells. The abnormal erythrocytes are sphere-shaped as opposed to being typically biconcave. This disorder is caused by mutations in genes responsible for production of membrane proteins that allow for the erythrocytes to change shape. Cells with these dysfunctional proteins can easily be degraded in the spleen, which causes hemolytic anemia. Symptoms include anemia, fatigue, jaundice and splenomegaly. Because of the hemolytic anemia indirect bilirubin accumulates in gallbladder and can cause pigmented gallstones and cholecystitis. Although research is ongoing, currently there is no cure for the genetic defect that causes hereditary spherocytosis. Disease management options include total or partial splenectomy and cholecystectomy.**

**Methods and materials: A case of a 17-year-old boy with right abdominal pain, dark urine, splenomegaly, vomiting and fever up to 39 degrees is described. Initially he is diagnosed with hemolytic anemia. After blood tests, abdominal ultrasound and Computed Tomography, consultations with a pediatric onco-hematologist and a surgeon the patient is diagnosed with hereditary spherocytosis with obstructive cholecystitis as a complication and suspected acute pancreatitis. Due to the increasing abdominal pain, nausea, vomiting and imaging findings, the patient is scheduled for planned cholecystectomy. Splenectomy was delayed due to the need for prior vaccination.**

**Results: After the operation, patient's general condition gradually improved. He is reported as afebrile, hemodynamically stable with physiological peristalsis. He is discharged surgically healthy for home treatment. Splenectomy will be scheduled after vaccination.**

**Conclusion: More researches are needed on the treatment of this syndrome and its complications. Experimental gene therapy to treat hereditary spherocytosis exists in lab mice, but this treatment has not yet been clinically tested in humans.**

**Keywords:** *hemolytic anemia, spherocytosis, cholecystitis, surgery*

# TROUSSEAU'S SIGN OF MALIGNANCY – A REPORT OF THREE CASES

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## ABSTRACT

**Introduction:** **Trousseau's sign of malignancy (TSM) is a paraneoplastic syndrome characterized by recurring and migrating episodes of thrombophlebitis. Named after Armand Trousseau, who first described it and considered it pathognomonic for malignant conditions, he subsequently self-diagnosed himself with it and died from gastric cancer. TSM most often leads to pulmonary thromboembolism (PTE) due to a detachment of thrombi and formation of emboli. TSM is associated with adenocarcinomas predominantly of pancreatic, gastric and lung origin.**

**Materials and methods:** **Three cases of migratory thrombophlebitis (MTP) are presented. All patients were treated at the St. Marina University Hospital, Varna, Bulgaria and referred for autopsy after death. The first case is of a 60-year-old male patient with acute gastrointestinal tract symptoms and history of recurrent thrombophlebitis for the past six months. The second case is of a 65-year-old female who three months prior to admission had suffered a PTE and was treated at a different institution. Current symptoms included respiratory failure, which was attributed to post-PTE changes. The third case is of a 73-year-old female with an adenocarcinoma of unknown primary origin, engulfing all the pelvic organs.**

**Results:** **The underlying cause of death in all patients was PTE with multiple thrombotic veins of the lower limbs, abdomen and abdominal wall. All patients also had an underlining malignancy – pancreatic adenocarcinoma in the first patient, pulmonary adenocarcinoma in the second and an adenocarcinoma of the ovary in the third.**

**Conclusion:** **The presented cases show the importance of TSM, both as a diagnostic tool in patients with discrete signs of malignancy and as an underlining cause of death in such patients due to the development of PTE.**

**Keywords:** *Paraneoolastic syndrome, Trousseau's sign, thrombophlebitis migrants, adenocarcinoma*

# ECTOPIC PANCREAS IN MECKEL'S DIVERTICULUM FOUND IN A FEMALE WITH INCARCERATED INTERNAL HERNIA

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## ABSTRACT

**Introduction:** **Ectopic pancreas is a pancreatic tissue found outside of the anatomic location of the pancreas as a rare condition. It is discovered incidentally and can be found in all organs of the gastrointestinal tract. Patients are usually asymptomatic. Clinical manifestations may include pain, inflammation, bleeding and/or obstructive syndrome.**

**Materials and methods:** **A 79-year-old female patient was admitted to the Second Department of Surgery of Saint Marina University hospital, Varna in severe general condition. She complained about four-day lower abdominal pain, followed by multiple episodes of nausea and vomiting. This clinical presentation led to the suspicion of an ileus. The patient has a history of total hysterectomy. Physical examination revealed pain in the lower abdomen, slow and missing peristalsis. Ultrasound findings included dilated small bowel loops (up to 32mm) filled with liquid. CT scan revealed a strangulated small intestine loop in the small pelvic. Oscillating peristalsis in the proximal parts of the small intestine, collapsed colon and minimal ascites were also observed.**

**Results:** **Despite the dangerously deteriorated general condition it was decided that the patient should be operated. Median laparotomy and debridement were performed due to postoperative adhesions. Around 200ml turbid liquid was drained and sent for microbiology testing which revealed ESBL producing bacteria resistant to all penicillins, all cephalosporins and aztreonam. The strangulated loop showed signs of necrosis therefore partial resection followed by latero-lateral anastomosis was performed. Part of the major omentum showed signs of dyscirculation and was excised. In the proximal jejunum a Meckel's Diverticulum with heterotopic pancreatic tissue was found and excised. Ten days later, after an uncomplicated postoperative period, the patient was discharged from the hospital in generally good health.**

**Conclusion:** **Asymptomatic heterotopic pancreas is rarely diagnosed. Even in asymptomatic patients it should be excised during a surgical procedure to prevent future complications.**

**Keywords:** *Ectopic pancreas, Meckel`s Diverticulum, Internal Hernia*

# MINIMALLY INVASIVE TREATMENT IN PATIENT WITH SPONTANEOUS ESOPHAGEAL RUPTURE DUE TO BOERHAAVE SYNDROME

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## ABSTRACT

**Introduction: Spontaneous esophageal perforation (EP) due to Boerhaave syndrome is a rear condition associated with high mortality, causing mediastinitis, empyema and sepsis if not diagnosed and surgically treated in the first 24 hours. This syndrome develops during or after persistent vomiting as a consequence of a sudden increase in intraluminal pressure in the esophagus. Minimally invasive surgical treatment for Boerhaave syndrome with VATS and adequate pleural drainage and esophageal stenting is presented.**

**Materials and Methods: 72-year-old male first admitted in the state hospital in Shumen with anamnesis of chest pain started after severe vomiting and clinical evidence for subcutaneous emphysema. On the chest X-ray was observed left sided hydropneumothorax. After emergency drainage of the left thoracic cavity, the patient was transferred to the Department for thoracic surgery of UMHAT "St. Marina" – Varna. The patient underwent computed tomography (CT) showing persistent hydropneumothorax, pneumomediastinum and chest tube above the level of the fluid. A decision for emergency VATS was taken. The content of the cavity was evacuated (mostly pieces of food), lavage with antiseptic solution of Iodine and physiological solution. The rupture was not sutured because signs for inflammation. A tube drainage was placed in the 7th intercostal space just above the diaphragm and second one in the 4-th used for lavage. Esophageal stent was placed on the level of rupture. The patient was discharged on the 30th postoperative day.**

**Results: In the following days the inflammatory changes disappeared, the patient was extubated, and his condition improved.**

**Conclusion: The Boerhaave syndrome is an emergency condition which could be treated minimally invasively.**

**Keywords:** *Boerhaave syndrome, spontaneous esophageal rupture, subcutaneous emphysema*

# GIANT LIPOSARCOMA LEADING TO HEMOPERITONEUM

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## ABSTRACT

**Introduction: Liposarcoma (LS) was first described by Rudolf Virchow in the 1860s. It is a malignancy of adipose cells - the most frequently occurring neoplasm of soft tissue, with a low incidence in adults. LS arises more often from deep stroma than from submucous or subcutaneous adipose tissue. It is predominantly situated in the limbs and the retroperitoneum and rarely the head and neck. LS is more common in men than in women.**

**Materials and Methods: A case of an 82-years-old patient, admitted to the emergency department of "St. Anna" Hospital, Varna with abdominal pain and swelling for the previous four to five days is presented. Clinical examination revealed severe asthenia and adynamia and frequent regurgitation, further questioning clarified that the symptoms had been present for a month. Laboratory findings included anaemia, leukocytosis, heightened levels of urea and creatinine. The patient had a history of ischemic heart disease, type two diabetes, benign prostate hyperplasia and hypertension. Medical imaging revealed air-fluid levels and a solid formation of unknown origin in the abdomen. Due to clinical and imaging signs of bowel obstruction, the patient was admitted at the First surgical department for conservative treatment.**

**Results: Following a lack of response to the therapy, emergency surgery was performed. Intraoperative findings included haemoperitoneum, two liters of fresh and old blood were aspirated. A large tumor formation with a rupture and bleeding, arising from the mesentrium of the small intestine was located and extirpated. Despite the application of a reanimation protocol in the intensive care unit, constant monitoring and anaemia correction, the patient passed away.**

**Conclusion: LS presents with no specific symptoms until the tumor reaches adjacent structures, causing pain and impeding organ function, sometimes fatally. LS develops slowly and manifests at late stages, when treatment is difficult and the risks - significant.**

**Keywords:** *Giant liposarcoma*

# PIN TRACT INFECTION AND ITS PREVENTION

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## ABSTRACT

**Introduction: Pin tract infections are a common complication of external fixation, complicating the healing process, often times requiring additional therapy and compromising treatment outcomes. Osteomyelitis or instability can result from pin loosening or complete construct removal.**

**Materials and methods: A literature review was conducted using the PubMed and Google Scholar databases. The search resulted in 24 articles after 2011, chosen based on their relevance to the topic. Pin sites are susceptible to infection due to skin disruption. Comorbidities such as diabetes, rheumatoid arthritis and other collagen vascular diseases, and use of steroids influence the risk of infection. Prevention includes prophylactic antibiotics, hydrogen peroxide cleaning, use of chlorhexidine-impregnated discs, dressing hygiene, all combined with the use of titanium pins and hydroxyapatite (HA) coatings.**

**Results: Increased duration of pin fixation as well as periarticular pin placement are both associated with a greater infection rate in comparison with diaphyseal placement. As a complication, infection is followed by pin loosening, fracture site contamination and also pain. Moreover, up to 4% of skin infections progress to intramedullary (IM) ones. Most pin site infections are treated with improved wound care and a short course of oral antibiotics. As expected, titanium improves the metal–skin interface by inciting a smaller inflammatory response. HA, on the other hand, enhances osseointegration of the pin and lowers the loosening rate - a major contributor to infection. In case of IM one, meticulous surgical debridement can prevent it from becoming chronic osteomyelitis.**

**Conclusion: The most frequent complication of external fixation is pin tract infection and associated osteomyelitis. Present comorbidities and prolonged duration of treatment in the fixator increase the risk of morbidity and premature removal of the metal components. The prevention consists of prophylactic antibiotic therapy, usage of titanium pins, coated with hydroxyapatite and proper hygiene methods.**

**Keywords:** *external fixation, pin tract infection, pin loosening, osteomyelitis, oral antibiotics, debridement*

# PERCUTANEOUS SUTURE OF ACHILLES TENDON RUPTURE

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## ABSTRACT

**Introduction: Rupture of the Achilles tendon has an incidence of 18 per 100000 and has been shown to be increasing due to a higher interest in physical fitness and athletic activity. Traditional open Achilles repair techniques have proven very effective but are not without drawbacks. This has led to the development of less invasive or percutaneous repair techniques that offer potential solutions for these problems. The Aim of this study is to analyze the results of a 13-year-long practice of the mini-invasive operative method and to compare it to its alternatives.**

**Materials and Methods: This study looks at data from the Dept. of Orthopedics, St. Anna Hospital, consisting of 438 patients with traumatic Achilles tendon rupture and we compare them to results from other studies. The cases date from 2006-2018. Follow-up is done in 295 of them according to Achilles Tendon Total Rupture Score (ATTRS). 244 patients were male, 51 female. Ages varied from 21-66 years, mean age of all pts: 42,9. Preoperative term: 0-14 days, on average 2 days. The percutaneous Achilles suture is accomplished in two layers through 10-12 skin incisions (5mm each), suturing by 2 threads; long straight needle (6cm); bellow knee plaster cast for 30 days, none-weight bearing; 24h postop hospital stay.**

**Results: Follow-up was done until 9 months after the surgery. Restoration of ankle amplitude on the 3rd month was reported in 235 (89%) pts. Re-ruptures in 13 (5%) pts. Superficial infections and skin necrosis 3 (1%) pts. Sural neuralgia 24 (9%) pts. Functional outcomes were with a mean ATTR score of 90, which is similar to results of other authors.**

**Conclusion: The Mini-invasive percutaneous suture of Achilles ruptures is a safer and more secure method with reduced patient morbidity and increased patient satisfaction in comparison to its alternatives.**

**Keywords:** *Achilles, Mini-invasive, Surgery*

# MINIMAL INVASIVE SCREW FIXATION OF PEDIATRIC ANKLE FRACTURES: A CASE SERIES

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## ABSTRACT

**Introduction: Pediatric ankle fractures comprise 5% of all fractures in children (1). The aim of this study is to compare the efficiency of Percutaneous Screw Fixation in comparison to Open Reduction and Internal Fixation(ORIF). ORIF requires extensive dissection and is often accompanied by wound complications such as infections, residual pain or malunion. (2)**

**Methods and Material: In total, 39 cases from "St. Anna" Hospital Varna, were reviewed and separated into two groups according to the performed treatment. Group 1 was treated with Percutaneous Screw Fixation, using cannulated partially threaded screws. The group consisted of 27 patients, aged 9 to 16 years (average of 11.48 years). Of those, 5 were male and 22 were female. The average VAS before surgery was 8.2 points and 3 months after surgery was 0.8 points. Group 2 was treated with ORIF. The group consisted of 12 patients in total, aged 10 to 15 years (average of 11.91 years). Of those, 3 were male and 9 were female. The VAS before surgery was 8.5 points and 3 months after surgery was 1.9 points. All patients were operated during the last 20 months (Stand: 11/2019).**

**Results: Both patient groups were compared according to the treatment outcomes. Patients of Group 1 showed less postoperative complications compared to those of Group 2. The VAS was 0.8 points and 1.9 points in Group 1 and 2 respectively. Radiographic imaging was obtained 1 month and 3 months after the initial operation. Screw removal was performed 3 months after the initial operation. The complete follow-up time was 6 months in all patients.**

**Conclusion: A comparison of both patient groups showed a better outcome in terms of healing and reduced postoperative complications in the group treated with Percutaneous Screw Fixation. In suitable patients this should be considered as the preferred treatment option.**

**Keywords:** *Percutaneous screw fixation, Pediatric ankle fractures, Ankle fractures, ORIF*

# EFFICACY OF TNF-A BLOCKING AGENT GOLIMUMAB IN PATIENTS WITH ACTIVE ANKYLOSING SPONDYLITIS

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## ABSTRACT

**Introduction: Ankylosing spondylitis still remains a topic of key discussion with difficulties arising in managing symptoms and improving prognosis. Golimumab, a tumour necrosis factor (TNF) inhibitor, has shown to relieve symptoms of some autoimmune disorders but to what extent it is effective as treatment shall be discussed.**

**The aim of the retrospective study is to analyze the efficacy of Golimumab as a main treatment in patients with active ankylosing spondylitis (AS) over a period of 24 months.**

**Materials and methods: Twenty patients with active AS beginning treatment in 2017 with Golimumab 50mg, injected subcutaneously every month were studied retrospectively. All 20 patients were controlled for HLA-B27 positive gene, of which 3 were females and rest male. Efficacy was evaluated using laboratory markers for inflammation such as erythrocyte sedimentation rate (ESR) and C-reactive protein (CRP). Disease specific scores: Bath Ankylosing Spondylitis Disease Activity Index (BASDAI) and Ankylosing Spondylitis Disease Activity Score (ASDAS) were also calculated at every visit.**

**Results: Evaluation of the results were made by analyzing the differences in the scores after the first and last visit and the values obtained of ESR and CRP of each patient during the visits. The results showed a mean decrease in ESR by 27.4% and CRP by 67.4% after all 5 visits. There was also a reduction in activity scores of 18.6% for BASDAI and 23.7% for ASDAS.**

**Conclusion: Golimumab is an effective method of treatment in patients with active ankylosing spondylitis for the alleviation of symptoms. Therefore, Golimumab is useful in sustaining the control of disease activity.**

**Keywords:** *Golimumab, ankylosing spondylitis*

# ARTHROSCOPIC TECHNIQUE OF TREATMENT IN FLEXOR HALLUCIS LONGUS TENOSYNOVITIS

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## ABSTRACT

**Introduction: Tenosynovitis of the m. flexor hallucis longus (FHL) appears as a result of chronic overuse or a change in the type or quantity of activity in training program. Tenosynovitis can be observed in Knot of Henry, under ligamenti Intersesamoidei, with a most commonplace occurrence on the medial malleolus.**

**Materials and methods: An in-dept literature review was conducted, using scientific articles from the databases: Sci-Hub, Sage Journals, PubMed and Google scholar. The article yield using the following words: arthroscopy, FHL, tenosynovitis was n=20. Articles were chosen based on the following criteria: published after 2010, pertinence to the topic. Tenosynovitis of FHL leads to a restriction of dorsiflexion in the first metatarsophalangeal joint clinically known as pseudo-Hallux rigidus. Retromalleolar pain is the main symptom, followed by swelling or clicking inside the ankle. MRI shows oedema and synovial swelling. In case of conservative treatment failure, the tendon is surgically released, usually done through an open procedure. Arthroscopic way of treatment is reviewed.**

**Results: The patients undergo posterior ankle arthroscopy. Two portals are made 1 cm above the Achilles tendon insertion, medially and laterally. A bursectomy follows in order to identify the FHL tendon. All fibrous tissue compressing the FHL is then removed and the tendon is released. No cast is applied as immobilization. The patient is encouraged to actively move the ankle and toes. The healing process includes 3 months of physiotherapy. The patients return to the same level of activity after a maximum period of 6 months.**

**Conclusion: Arthroscopic treatment is a minimally invasive technique to treat FHL tenosynovitis. The arthroscopic approach, with a steep learning curve, demands skills but avoids the aggressive open technique. The former shortens the period of recovery, in comparison to the latter. The lack of immobilization speeds up patient healing while lowering the hospital stay period.**

**Keywords:** *Arthroscopy, flexor hallucis longus tenosynovitis*

# OSTEOBLASTIC OSTEOSARCOMA OF THE RIGHT TIBIA – CASE REPORT

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## ABSTRACT

**Introduction: Osteoblastic osteosarcoma (OO) is a rare osteoid-forming spindle cell neoplasm, predominantly occurring in adult males. It typically presents with exclusively orthopedic symptoms in advanced disease. Diagnosis is further made more difficult by the many subtypes and different radiological signs of the disease.**

**Materials and methods: A 74-old woman with severe pain and dysfunction of the right leg presented at Orthopedics and Traumatology department at University Hospital Saint Marina – Varna. Previous conservative treatment had proven to be ineffective. Due to a suspected neoplasm X-ray imaging was conducted. The data yielded was interpreted as transformation of Paget's disease into osteosarcoma. A tissue biopsy followed, which confirmed the condition as OO arising from Paget's disease. These findings led to the decision to conduct local bone excision as a curative procedure.**

**Results: A local excision of the lesion in the tibia was conducted under general anesthesia. An area of necrosis was discovered during the procedure and a tissue sample taken, as well as a 1x1 cm bone cube, which were sent for further histopathological classification. Said sample confirmed the initial diagnosis. The operation was followed by a standard protocol of Fraxiparin and Methamizole as well as physical rehabilitation. Restaging was conducted by Positon-emission tomography/ Computed tomography (PET/CT), which showed a large heterodense formation with pathologically elevated glucose metabolism, affecting the distal third of the tibial diaphysis and the epiphysis, as well as the underlying musculature, with dimensions: 45mm axially and 120 cranio-caudally. In addition, two nodular lesions with low metabolic activity were discovered in the right lung, that were suspected metastases. Further operative treatment was conducted – amputation. PET/CT showed no pathological metabolic activity following the procedure.**

**Conclusions: The typical presentation of the disease resembles more benign conditions, especially in younger individuals. Care should be taken to exclude OO as a potential diagnosis.**

**Keywords:** *neoplasm, osteoblastic osteosarcoma, Paget's disease, amputation*

# EVIDENCE BASED "GOLD STANDARD" FOR INGUINAL HERNIA IS STILL THE LICHTENSTEIN HERNIOPLASTY

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## ABSTRACT

**Introduction: A large number of studies and national hernia registers have confirmed, with high levels of evidence that the placement of permanent synthetic fabric is significant and reduces the possibility of recurrence in operations on inguinal hernias. Since it has been published in 1986 by Irving L. Lichtenstein, the concept of "stress-free recovery" is rapidly expanding globally. Nowadays, primary symptomatic unilateral hernias should be treated with TAPP (transabdominal peritoneal access) or TEP (total extraperitoneal access) and bilateralhernias should be approached laparoendoscopically. Usually, the "Lichtenstein" technique is successfully performed under local anesthesia and is less complex in terms of the equipment required, in comparison with laparoendoscopic surgery.**

**Materials and methods: We have combined our experience with inguinal hernias and systematic review based on an extensive literature search of Pubmed, Medline, The Dutch Cochrane database, Hernia The World Journal of Hernia and Abdominal Wall Surgery and International guidelines for groin hernia management.**

**Results: According to the World Guidelines and all of the noble names in the hernia society the Liechtenstein hernioplasty continues to be the preferred method for primary unilateral inguinal hernias (TAPP and TEP equivalent), large scrotal hernias and recurrences after laparoendoscopically operated inguinal hernias. Laparoendoscopic techniques are preferred to bilateral hernias, femoral hernias and recurrent ones after anterior access.**

**Conclusion: The aim of this article is to describe Liechtenstein's actual technique and to discuss its background and weaknesses that lie with the evidence. Our goal is to evaluate Lichtenstein inguinal hernioplasty as the "gold standard" for open approach repair.**

**Keywords:** *Lichtenstein, hernioplasty, hernia*

# VARIA

# NON-INVASIVE PRENATAL SCREENING BY PRENATEST: FIRST CHOICE FOR CHROMOSOMAL ANEUPLODIES

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## ABSTRACT

**Introduction: Non-Invasive Prenatal Screening (NIPS) is a diagnostic tool that evaluates the risk of a fetus being born with certain genetic abnormalities. It is done by taking a sample of venous blood from mother and studying the presence of fetal cfDNA. This study investigates the benefits of it as a diagnostic tool. To assess the need for amniocentesis; an invasive and riskier procedure. Which will be confirm Downs, Edwards and Pataus.**

**Materials and Methods: 365 pregnant women, between the years 2012-2019, were given NIPS at St Marina Hospital, Varna. Their maternal age, gestational age, reason for referral and presence of chromosomal aneuploidy was investigated. The median gestational age was 12 weeks. Most patients came in out of personal choice and/or due to some discrepancies in previous screening methods.**

**Results: The hospital records from the genetic investigations showed 83 out of 365 patients were referred due to discrepancy in biochemical screening. Nn further analysis with PrenaTest, only 2 of the cases showed actual evidence of trisomy 21. 97 out of 365 patients were referred due to maternal age being over 35. After NIPS, only 3 out of the 97 showed evidence of trisomy 21 and 1 showed evidence of trisomy 18. The remaining chromosomal aneuploidies were due to a multitude of other factors.**

**Conclusion: Biochemical screening results and actual presence of chromosomal aneuploidy had a weak correlation; due to low sensitivity of biochemical testing, compared to PrenaTest. NIPS by PrenaTest has the highest sensitivity for Downs Syndrome (99.3%), Edwards (97.4%) and Patau (97.4%). NIPS by PrenaTest is suitable for all patients; with differing histories, complications, backgrounds and needs. It is 100% safe to both the pregnant woman and the fetus, non-invasive and has rapid test result, therefore more accessible for all who desire genetic investigation, when it comes to pregnancy and starting a family.**

**Keywords:** *prenatal screening, chromosomal aneuploidies, non-invasive*

# E-CIGARETTE OR VAPING PRODUCT USE ASSOCIATED LUNG INJURY (EVALI) – WHAT WE KNOW SO FAR

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## ABSTRACT

**Introduction: E-cigarette or vaping product use associated lung injury (EVALI) has emerged as a global health issue this year with more than 2000 cases and over 40 deaths reported worldwide. The aim of this review is to clarify the etiology, pathogenesis, clinical features, diagnosis and treatment of EVALI.**

**Materials and methods: Scientific articles were gathered via PubMed and Scopus using the keywords: e-cigarettes; vaping; lung injury with only articles written in 2019 being selected.**

**Results: EVALI is most often caused by the use of tetrahydrocannabinol (THC) containing products and nicotine-containing products, but no single compound or ingredient has emerged as the cause of EVALI to date. The pathogenesis of EVALI in humans is still unknown, but studies in mice have found that e-cigarette vapor inhibits DNA repair in lung tissues. Histhopathological findings include acute eosinophilic pneumonia, diffuse alveolar hemorrhage and lipoid pneumonia, suggesting that more than one mechanism of injury may be involved. Clinical manifestations of EVALI include cough, chest pain and shortness of breath, often accompanied by gastrointestinal (abdominal pain, diarrhea, nausea and vomiting) and constitutional (fever, chills and weight loss) symptoms. Physical examination reveals tachycardia, tachypnea and decreased blood oxygen saturation (<95%). EVALI is considered a diagnosis of exclusion because at the present time there is no specific test or marker. It is important to exclude any underlying infectious disease – influenza, S. pneumoniae, L. pneumophila, M. pneumoniae, etc. Radiographic findings include pulmonary infiltrates on chest X-ray and opacities on chest CT. Currently, there is no available treatment, but several case reports described improvement with corticosteroids.**

**Conclusion: EVALI is an emerging, potentially life-threatening condition. Based on the current scientific consensus on the topic and lack of specific clinical or histological hallmarks, further studies are needed to establish the pathogenetic mechanisms and long-term consequences of e-cigarette use.**

**Keywords:** *e-cigarettes, vaping, lung injury, pulmology*

# WARNINGS AND PRECAUTIONS IN THE PATIENT INFORMATION LEAFLET

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## ABSTRACT

**Introduction: The patient information leaflet (PIL) is a major technical document included in every medicine package with the main purpose to inform patients about their medication regarding administration, precautions and potential side effects. Column warnings and precautions include drug interactions, intake with food and drinks, pregnancy and breast-feeding and driving and using machines. There are pregnancy categories of a medication which is an assessment of the risk of fetal injury due to the pharmaceutical if it is used as directed by the mother during pregnancy. The aim is to analyze some specific data presented in PIL of 5 main anatomical/pharmacological groups from 1st level of ATC classification and to determine is it enough information from patient information leaflet for safe drug use during pregnancy and while driving.**

**Materials and methods: The study contains comparative analysis of extracted and summarized information from PIL of 1200 drugs from the ATC anatomical groups: A- Alimentary tract and metabolism, B- Blood and blood-forming organs, C- Cardiovascular system, D- Dermatologicals, G- Genito-urinary system and sex hormones. The following criterions were included in our research - pregnancy intake and influence on the ability to drive and use machines.**

**Results: Only 7,21 % of medicines may be taken during pregnancy. 44,5% should not be taken during pregnancy, 20% need to consult before taking and 14% had no studies according to patient information leaflet. In the PIL is not describing which category from the classification of WHO are the medications. Almost half (47%) of the drugs can change the ability to drive and use machines, 37% cannot change the ability to drive and 9 % had no clinical studies.**

**Conclusion: All these results lead to the conclusion that the information from the PIL is not enough and medical consultation is a very important part of safe drug use.**

**Keywords:** pregnancy, patient leaflet, driving, information

# SEROPREVALENCE OF TOXOCARIASIS IN CHILDREN AND ADULTS OF NORTHEASTERN BULGARIA

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## ABSTRACT

**Introduction: Human toxocariasis is a helminthic zoonosis caused by larval stages of Toxocara canis and Toxocara cati. Contamination of the environment with helminth eggs from cats' and dog' feces is the key route of transmission. Humans contract the infection by ingesting embryonated eggs. There are four forms of the disease – covert, visceral larva migrans, ocular and neurotoxocariasis. The aim of this study is to establish the levels of seroprevalence of toxocariasis among children and adults in Northeastern Bulgaria.**

**Materials and Methods: Included in the current investigation is an actively selected group of 30 children and 51 adults with symptoms specific for the Toxocara infection (allergic reactions, rhinorrhea, ocular disturbances, cognitive disorders, epilepsy, iron-deficiency anemia, eosinophilia, ect.) and control group of randomly selected 61 healthy individuals. The seroprevalence of anti-Toxocara antibodies is determined by ELISA, followed by verification of the ELISA-positive findings with Western blot (WB).**

**Results: The preliminary ELISA tests showed 30 positive results and only 19 were confirmed with WB for the presence of specific anti-Toxocara antibodies. This results in an overall seroprevalence of 13.38% (19/142) in the investigated population. The rates demonstrated in children 10.00% (3/30) and adults 13.73% (7/51) with clinical symptoms corresponds with the increased environmental exposure over time. The highest result of 14.75% (9/61) in the group of healthy controls validates the mild and asymptomatic, hence "covert" course of toxocariasis, especially in adults.**

**Conclusion: ELISA essay is a suitable test for initial investigation of a large number of people but the observed cross-reactivity, demands verification of with more specific immunological methods like WB. The background seroprevalence of toxocariasis in Norteastern Bulgaria is significantly high and exceeds 10% in all the investigated groups. This demonstrates that the essentially unknown Toxocara-infection presents a considerable public health problem that requires further investigation and increased awareness.**

**Keywords:** *Toxocariasis, Toxocara infection, ELIZA, Western blot*

# EXPLORATORY RESEARCH OF THE STANDARD TERMS LIST IN EUROPEAN PHARMACOPOEIA

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## ABSTRACT

**Introduction: European Pharmacopoeia is a primary document which provides official quality standards for the pharmaceutical industry in Europe and it is essential tool for the control the quality of medicines and the substances used to manufacture them. One of its basic functions is to serve public health. The list of Standard Terms was initially drawn up by the special Working Party following a request of the European Commission, for use in marketing authorization applications, labelling (including the summary of product characteristics), and electronic communications.**

**Materials and Methods: We performed an exploratory research with benchmark analysis of the list of standard terms, actual until October 2019, which is available online on the official website of EDQM. We also perform a comparative sorting of the standard terms in different categories by several criteria which are Methods of administration and Basic dosage form.**

**Results: The results demonstrate that up to the moment there are 476 terms in the list of European Directorate for the Quality of Medicines & HealthCare Routes and Methods of Administration Terminology. Out of all terms for pharmaceutical dosage form included in the Bulgarian list of standard terms 32 % are related to dosage forms for Oral use, 12% are meant for Injection use. Other methods of administration with significant percentage are Infusion and Application to the skin each with 7%. Only 4% of all dosage form have no applicable route of administration.**

**Conclusions: Standardization of terms is a very important aspect in pharmaceutical regulation. When an appropriate standard term is established, its use should start immediately. Standardization is a key principle in insuring quality of medicines.**

**Keywords:** *Standard Terms; Route of administration; European Pharmacopoeia*

# RADIOPHARMACEUTICALS – EVALUATION OF DRUG SAFETY SYSTEM IN BULGARIA

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## ABSTRACT

**Introduction: Radiopharmaceutical drugs are specific therapeutic drugs that recently have become important for innovative therapeutic approach and diagnostics. These medicinal preparations consist of a substance which, by their physico-chemical characteristics, can be applied either for therapeutic or for diagnostic purposes. Radiopharmaceutical drug intake is associated with radiation risk and adverse reactions. The aim of the study is to study the methods of pharmacovigilance system as a drug safety evaluation in Bulgaria and to explore the most common ADRs related to therapy or diagnostics with radiopharmaceuticals.**

**Materials and methods: A review of information data from available literature sources is held based on keywords radiopharmaceuticals, pharmacovigilance, ADR, drug safety using search engines PubMed, ScienceDirect, Springer, Embase, Scopus, and GoogleScholar. We emphasize on drug safety systems as an instrument for implying pharmacovigilance principles and the role of medical professionals in the process in reporting ADRs.**

**Results: The Bulgarian Drug Agency (BDA) is the only national competent authority currently receiving ADRs reports. There are four ways of reporting ADRs including web-based form, MAH report, e-mails(letter) and national phone line. Adverse reactions to RPs are comparatively rare. Patients tend to contact the MAH rather than the executive state agency. The role of medical professionals– especially of the pharmacist, and MAH is highly important for effective signal registrations. According to the WHO, healthcare professionals "maintain health in humans through the application of the principles and procedures of evidence-based medicine and caring".**

**Conclusion: There is a meager amount of data available regarding the adverse effects associated with radiopharmaceuticals. Many adverse effects associated with radiopharmaceuticals are not reported due to the lack of awareness about the reaction, improper reporting system, and overall poor reporting culture. Whereas reporting of adverse effect and sharing of information may minimize the incidence of adverse effects associated with radiopharmaceuticals.**

**Keywords:** *radiopharmaceuticals, pharmacovigilance, ADR, drug safety*

# USE OF OCTREOTIDE AS MANAGEMENT OF CHYLOUS ASCITES IN PAEDIATRIC PATIENTS

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## ABSTRACT

**Introduction: Octreotide is a somatostatin analogue administered subcutaneously in chylous ascites. It reduces lymphatic flow by decreasing the absorption of lipids from the intestine into the lymphatic system. Currently, there is no standard treatment of chylous ascites. Chylous ascites is a rare condition caused by accumulation of chyle in the peritoneal cavity. The aim of this review is to discuss the effectiveness of octreotide, as management of chylous ascites in paediatric patients, using case studies of patients, published from 2012-2019.**

**Materials and Methods: The sources that were used are PubMED, BMJ, ResearchGate and Medscape, to find studies that showed the success or failure of octreotide for the management of chylous ascites in paediatric patients and any limitations there might be to its use. The 12 case studies that were used analysed the treatment with octreotide in paediatric patients which involved varying etiological reasons for chylous ascites. They all followed a combination therapy of octreotide, total paraenteral nutrition and medium-chained triglyceride diet as part of the treatment.**

**Results: The results showed that octreotide successfully treated chylous ascites in all case studies of paediatric patients. Additionally, octreotide was effective by reducing the number of days to resolve chylous ascites, which meant hospital stay was shorter. None of the case studies presented any adverse effects in the treatment with octreotide, which proves it to be a safe drug for patients. Additionally, some studies showed that the dosage did not have much effect in the treatment either. It was found that all of the paediatric patients responded similarly to the treatment of chylous ascites.**

**Conclusion: To conclude, the usage of octreotide in the treatment and management of chylous ascites in a clinical setting show reliable and consistent results and therefore could be used as a standard treatment for all cases of chylous ascites in paediatric patients.**

**Keywords:** *Octreotide, Chylous Ascites*

# THE CHALLENGES OF TREATMENT-RESISTANT SCHIZOPHRENIA

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## ABSTRACT

**Introduction: Treatment-resistant schizophrenia (TRS) is a neuropsychological disorder, in which patients can hardly achieve remission with antipsychotics over a prolonged period. Moreover, a failure of response to two separate adequate trials of antipsychotics is required for the diagnosis. Clozapine is the golden standard for TRS. Nearly 30% of people with schizophrenia are affected.**

**Materials and methods: A case report of a 36-year-old man with TRS hospitalized in University Multiprofile Hospital for Active Treatment "St. Marina"-Varna. The disorder was diagnosed 14 years ago with a display of insomnia, psychotic behavior and negative symptoms (NS) – social withdraw, depression with suicidal tendencies and a suicide attempt. Due to a partial response to treatment, as well as its bad management, the patient started developing positive symptoms (PS) like sound pseudohallucinations and paranoia. Since the subject could not achieve full remission with the prescribed medications, his disorder progressed rapidly.**

**Results: In correlation to the persistent PS, the patient has a documented failure of response for more than 6 weeks to more than 2 antipsychotics (Amisulpride, Risperidone, Chlorpromazine Hydrochloride, etc.) with a dosage higher than 600 Chlorpromazine equivalents. As none of the prescribed drugs accomplished a full remission, the incorporation of Clozapine is mandatory. The Initial dose is 12.5/25 mg and it should be titrated gradually. Nevertheless, there are many side effects like sialorrhea, seizures, hypotension, agranulocytosis, which are dose-related and need to be monitored. Despite the subject's poor mental health, he declined the Clozapine treatment. His condition has not improved.**

**Conclusion: The objective is to present the importance of the administration of Clozapine therapy, as it's the only medication licensed for TRS. The reported case highlights the need for the development of even more low-risk RST treatment guidelines.**

**Keywords:** *treatment-resistant, schizophrenia, psychiatry, Clozapin*

# GOLDENHAR SYNDROME

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## ABSTRACT

**Introduction: Goldenhar syndrome or hemifacial microsomia is a congenital condition represented mainly by underdeveloped eye and ear (with atresia of the external ear canal) or the total absence of them, spine malformations and non-malignant eye growth (ocular dermoid cyst), causing the most characteristic sign of the disease – the facial asymmetry. Hearth, lungs and kidneys may also be affected. These abnormalities are caused by an irregular development of the first and second brachial arches, from which these structures are derived from, but the exact etiological reason is yet unknown.**

**Materials and Methods: A case of a 7-year-old boy born with multiple anomalies – unilateral facial hypoplasia, left ear hypoplasia, bilateral preauricular skin tags, lagophtalmos, hearth malformation. Further examination showed atresia of the external left ear canal, underdevoleped tympanum with congenital defect of the inner ear, that all together with audiometric analysis indicate total loss of left ear auditory capabilities. X-ray of the skull showed unicoronal synostosis that leads to disproportional growth of the brain. The patient was clinically diagnosed with the syndrome.**

**Results: Uncommon by this patient regarding the typical signs of this condition is the appearance of some further abnormalities in the left lower extremity. Talipes equinovalgus, preaxial foot polydactyly are the externaly noticeable malformations. The following X-ray of the leg revealed absence of fibular bone, hypoplastic tibia and a sixth phalanx. A surgical intervention was made to remove the excess structures.**

**Conclusion: This example of Goldenhar syndrome adds to the symptoms typical for this condition. Genetic confirmation of the syndrome is not possible because of unknown etiology, but accurate clinical diagnosis enables adequate genetic counseling of the family and determining the recurrence risk.**

**Keywords:** *Goldenhar syndrome*

# RISK FACTORS INFLUENCE-ORAL HYGIENE AND TOOTH DECAY IN RISK ASSESSMENT FOR CHILDREN FROM 3 TO 18 YEARS

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## ABSTRACT

**Introduction: Tooth decay is a multilateral disease that develops in result of simultaneous and mutual effect of a group of factors. Nowadays tooth decay is considered "behavioral disease with bacterial involvement". The aim of this study was to assess the tooth decay development in children from three to eighteen years and some risk factors influencing like oral hygiene and carious lesions presence.**

**Materials and Methods: The research was carried out at the Faculty of Dental Medicine - Varna. The number of children participated in the study was thirty (n= 30), aged from tree to eighteen. Children were examined with a history and detailed registration of clinical status which was done by using dmft/DMFT index. Scientific data is collected by SPSS v.19 mathematical software package. The risk of caries of deciduous and permanent teeth was evaluated.**

**Results: The research showed that the percentage of children suffering from tooth decay is higher. From 30 tested children patients 23 have shown caries lesions as well as tooth fillings up until the initial clinical examinations of the research dmft(T)= 23. Seven of the thirty tested children patients were not suffering from dental decay or had tooth fillings up until the initial clinical examinations dmft(T)= 7. Data analysis from using risk assessment instrument have shown that 83% of children tested were of high risk of tooth decay and only 17% were of low risk of tooth decay.**

**Conclusions: The high percentage of irreversible and active caries lesions means that the oral environment is highly cariogenic. From the research risk factors for patients 3-18 years old like level of oral hygiene and tooth decay show proportional dependence. After risk assessment individual programs for every tested patient are made for prophylaxis and non-invasive treatment in children's age.**

**Keywords:** *tooth decay, oral hygiene, risk assessment*

# ANALYSIS OF THE OPPORTUNITIES FOR OBTAINING A PHD DEGREE IN BULGARIA

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## ABSTRACT

**Introduction:** **In Bulgaria, doctoral programs are distributed in 9 different domains of Higher Education, consisting of 51 strands in accordance with current trends and realities in science and academic development training, related to the achievements of science, the requirements of national and international standards for quality of education and universal values.**

**Methods and materials:** **Public data in the official website of the National Agency for Evaluation and Accreditation of all Bulgarian universities and scientific organizations accredited for the respective PhD program was analyzed. A focus was put on the Healthcare and Sports domain. The criteria by which the Universities and the Scientific organization were compared were; the number of programs in different fields and areas; the average score of each area and direction, including the average score for all accredited programs; the number of new and dropped-out programs in specific universities. The comparison was made by the Z score method.**

**Results:** **The obtained results showed that in Bulgaria there are doctoral programs in all 9 domains of higher education with a possibility to be obtained in 43 Universities (a total number of 51 as 8 are without accreditation) and in 15 Scientific organizations. A glut of programs was observed in the domains: 3. Social, economic and legal sciences - 496 programs in 9 directions and 5. Technical sciences - 482 programs in 13 directions, respectively with a total number of all programs - 2211.**

**Conclusion:** **Research is a part of the curriculum in most of the universities and they offer various PhD programs to support it. In Bulgaria, Doctoral studies are offered in all fields of science and they are performed by universities or Scientific organizations accredited for their respective program. Domain 7. Healthcare and Sports is subjectively currently immature in relation to the number of PhD programs offered in it.**

**Keywords:** *PhD, Scientific organizations, Doctoral studies, science, Healthcare and Sports*

# RADIOPHARMACEUTICAL RADIUM-223 AND ITS ROLE IN THE TREATMENT OF PROSTATE CANCER

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## ABSTRACT

**Introduction: Prostate cancer is one of the most common types of cancer in men. In many cases it may not cause serious harm. Some types of prostate cancer grow slowly and may need minimal or even no treatment, other types are aggressive and can spread quickly. Castration-resistant prostate cancer (CRPC) is an advanced form of neoplasm of the prostate, not suitable to surgical treatment. Typical for this tumor is that it keeps growing even when the amount of testosterone in the body is reduced to very low levels. Once a patient enters a castration-resistant state, he is more likely to die of his prostate cancer than of other causes. The development of bone metastases and subsequent symptomatic skeletal events significantly reduce survival and quality of life.**

**Materials and methods: A retrospective analysis through popular scientific databases was performed using pre-defined keywords.**

**Results: Radium-223 dichloride (Xofigo), formerly alpharadin, is an alpha-particle–emitting radioactive therapeutic agent that was approved by the FDA in May 2013 and by EMA in November 2013. It is approved for men with CRPC, symptomatic bone metastases, and no known visceral metastatic disease. The published data indicate that this radiopharmaceutical have a potent targeted antitumor effect and the clinical trials showed both a survival benefit and good safety profile, including limiting chronic radiation exposure to the patient. Radium-223 provides a new treatment option for this setting, but also necessitates a new treatment management approach. The approved dose regimen is an activity of 55 kBq per kg body weight administered by six intravenous (IV) injections at 4-weekly intervals.**

**Conclusion: Nuclear medicine now plays an increasingly important role in the management of patients with CRPC. Radium-223 is the first targeted alpha therapy with antitumour properties and proven significant survival benefits in men with CRPC and bone metastases.**

**Keywords:** *Prostate cancer, pharmacotherapy, radium-22*

# CD34 PROGENITOR CELLS IN MULTIFORM GLIOBLASTOMA

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## ABSTRACT

**Introduction: Glioblastoma multiforme (GBM) is a World Health Organization (WHO) grade IV malignant tumor with astrocytic differentiation. The yearly incidence of GBM in the north-eastern Bulgarian population is 3 cases per 100 000 capita. Despite medical advances over past few decades the life expectancy of patients has remained relatively unchanged – 8 to 12 months. There are two proposed mechanisms for the development of GBM - natural progression of lower grade astrocytomas and de novo arisal. Both of these theories however center on neural progenitor cells in the central nervous system.**

**Materials and methods: Fourteen cases of tumors with astrocytic differentiation were evaluated using the automated immunohistochemistry (IHC) detection algorithm of Qupath v0.2.0-m4. Due to CD34 marking not only neural progenitors, but endothelial cells as well, the tumors were evaluated over an area of 76 square millimeters, with blood vessels excluded from the analysis. In superficial tumors, again an are of 76 square millimeters was evaluated in the subpial one. The data and patient survival were analyzed for statistical significance with MedCalc v19.1, using the Kaplan-Meier method with differences assessed by the log-rank test. Case corresponding 95% confidence rates were estimated by Cox regression modelsand two tailed p-values ($p<0.05$) were considered as statistically significant.**

**Results: The tumors included 11 GBMs, two gliosarcomas and one WHO grade II astrocytoma, due to the small sample size, only the GBMs were subjected to a statistical analysis. Both the hotspot ($p=0.076$) and subpial ($p=0.243$) values did not show correlation with patients' survival with borderline expression being defined as 3.6%.**

**Conclusion: Despite the specific patterns of growth and diffuse spread of CD34 progenitors, their percentage does not correlate with patient's survival.**

**Keywords:** *Glioblastoma multiforme; CD34; progenitor cells*

# PREVALENCE OF TUMOR GROWTH PATTERNS AND PATHOGNOMONIC FEATURES IN CENTRAL NERVOUS SYSTEM TUMORS WITH ASTROCYTIC DIFFERENTIATION

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## ABSTRACT

**Introduction: Gliomas are the most common primary malignant central nervous system (CNS) tumors. The World Health Organization (WHO) has a specific set of criteria on grading gliomas from WHO grade I to IV. The grading is predominantly carried out on hematoxylin and eosin stained slides based on specific histological characteristics and patterns. The aim of this study was to establish whether a correlation exists between the presence of primary and secondary Scherer structures, WHO grading and the natural progression of tumors with astrocytic differentiation.**

**Materials and methods: Patients diagnosed with CNS tumors with astrocytic differentiation in the St. Marina University Hospital, Varna, Bulgaria for a period of one calendar year February 2018 – March 2019 were included into the study. Tumor samples were analyzed for the presence of primary Scherer structures – pseudopalisadic necrosis, glomeruloid vascular proliferation and secondary Scherer structures – subpial palisading, tractal aggregation, satellitosis around neurons and blood vessels.**

**Results: A total of 28 Glioblastoma Multiforme (GBM) cases were included in the study. All of these tumors (100%) had the patogmonomic primary Scherer structures (pseudopalisadic necrosis) and perivascular satellitosis (100%). Glomeruloid vascular proliferation was observed in 89.29%, perineuronal satellitosis in 96.42%, subpial palisading in 67.86% and tractal aggregation in 78,54% of cases. A total of eight other cases were diagnosed as lower WHO grade gliomas as they did not have primary Scherer structures and glomeruloid vascular proliferation. These tumors however had perivascular satellitosis in (100%), perineuronal satellitosis (100%), subpial palisading (50%) and tractal aggregation (87,5%).**

**Conclusion: Primary and secondary Scherer structures are the natural growth pattern of glial tumors with astrocytic differentiation. Only the primary structures can be considered pathognomonic for GBM.**

**Keywords:** *Pathology, CNS tumors; Glioma, Scherer structure*

# ROLE OF TRANSCRIPTION FACTOR ZBTB20 IN THE CEREBELLAR CORTEX DEVELOPMENT

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## ABSTRACT

**Introduction: The transcription factor Zbtb20 is important for the hippocampal, neocortical and liver development. However, its role in prenatal and postnatal cerebellar development has not yet been elucidated.**

**Materials and Methods: Here we investigated the effect of the transcription factor Zbtb20 on thecerebellar Purkinje cells during postnatal (P) development. We used wild type (WT) and Zbtb20knockout mice (Zbtb20KO) mice aged at postnatal days P4, P8, P12. Brain sections were immunostained for calbindin (CB), a calcium-binding protein that selectively markers Purkinje neurons in the cerebellar cortex.**

**Results: Immunofluorescent staining revealed that at P4 the highest number of CB-positive cells, both in mutants and controls, was in folia III and IV of the cerebellar cortex, while the lowest number was found in folium I. However, the number of CB-positive cells in the mutants was higher compared with the controls, and this tendency was preserved at P8 andP12. Cerebellar growth and lobulation continues at least up to P12 in both controls and mutants. At P12, a greater number of CB-positive cells were detected in the III, IV, VI and VII folia of the mutants, than in the controls. There was no significant difference in the foliation between the two experimental groups.**

**Conclusion: These results indicate, that Zbtb20 plays a role as a regulator of the development of cerebellar Purkinje neurons.**

**Keywords:** *Cerebellum development, Calbindin, transcription factor, Zbtb20, Purkinje neurons*

# DIAGNOSTIC TOOLS FOR DETECTION OF CARDIOTOXICITY – A METHODOLOGICAL REVIEW

**Nikolai Borisov Kalvachev[1], Svetoslava Slavcheva[2], Maria Vetkova[2], Petar Petrov[2], Atanas Angelov[2]**

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## ABSTRACT

**Introduction:** **Chemotherapy-induced cardiotoxicity is the biggest non-cancer cause of late mortality in cancer survivors. The most common presentation is heart failure. The need for early subclinical detection is paramount since it often affects the outcome for the patient.**

**Materials and Methods:** **The aim of this review is to highlight the possible uses of novel biomarkers and visual modalities. A systematic review of the literature was conducted for the period 2019-2015, through the database of PubMed, Google Scholar, Scopus. Keywords like cardiotoxicity, biomarkers, diagnostic modalities, chemotherapy were used. Forty-seven articles were included in the final review. Exclusion criteria included non-human research, case reports, letters etc.**

**Results:** **Serum biomarkers can be used for early detection of the probability of cardiotoxicity, before clinical manifestation. Cardiac troponins release is the earliest sign. However peak values occur at different times. Together with NT-pro BNP they are the most persistently used biomarkers with consistent positive correlation. There is no threshold value for risk stratification. Increased micro RNA expression can also be an early sign, although they are still not routinely used. The predictive value of myeloperoxidase and high-sensitivity C-reactive protein is currently debatable. Antracycline-naïve patients may be missed by currently used serum biomarkers. Imaging modalities can detect cardiotoxicity only after cardiac injury or dysfunction is established. The echocardiography is recommended for assessment of left ventricular ejection fraction, valvular and pericardial complications and pulmonary hypertension. Global longitudinal strain is an early predictor of subsequent cardiotoxicity. The cardiac magnetic resonance is preferred for structural evaluation and in patients not assessable by echocardiography.**

**Conclusion:** **Cardiotoxicity is a growing clinical problem and early detection is the key to primary prevention and decreased mortality rate. There are a wide asset of biomarker assays and visual modalities, however there is still no uniform approach. A multimodal strategy combining both methods is preferred.**

**Keywords:** *Cardiotoxicity, Chemotherapy, Serum biomarkers, Imaging modalities*

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### Book

Murray PR, Rosenthal KS, Kobayashi GS, Pfaller MA. Medical microbiology. 4th ed. St. Louis: Mosby; 2002.

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Zhang M, Holman CD, Price SD, Sanfilippo FM, Preen DB, Bulsara MK. Comorbidity and repeat admission to hospital for adverse drug reactions in older adults: retrospective cohort study. BMJ. 2009 Jan 7;338:a2752. doi: 10.1136/bmj.a2752. PubMed PMID: 19129307; PubMed Central PMCID: PMC2615549

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