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THERAPY – WERE TO?*

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Background and Aims. An infection with *Clostridium difficile* has suggestive symptoms and predisposing factors such as age, previous antibiotic treatment, winter season, immunosuppression, major chronic diseases, Intensive Care Units ICU admittance. Because in terms of age Arad County has a certain rate in change of population over 60 years and excessive antibiotic treatment is still recommended to all ages for outpatients, we assessed the incidence of these infections and post-therapy antibiotic relative risk for all assisted cases in Arad County Emergency Hospital between 2013-2014.

Material and method. Were analyzed *Clostridium difficile* infections recorded in 2013-2014 in terms of their incidence in hospital wards, seasonal distribution, gender and age, underlying disease and related diseases, using *SPSS 14.0 for Windows* and *MedCalc* for statistical data processing.

Results. There were 42 infections with *Clostridium difficile* in hospitalized patients, with average age of cases 66 years, SD =13.97, Gender ratio F/M 1.21. Monthly distribution is ubiquitous, with minimum in summer and maximum in spring and autumn, their occurrence being reported by eight wards of Arad County Emergency Hospital. Highest incidence for 2013 were 15.36% in the pneumology department with minimum 0.67% for gastroenterology, and for 2014 these infections were present in surgical wards, ICU and adult infectious disease, with incidences between 3.01-2.61%, minimum 0.43% in gynecology wards. The underlying disease for which these patients were assisted initially mainly affected digestive and respiratory system, and comorbidities were chronic cardiovascular diseases at the rate of 45.24%. With previously antibiotic treatment before *Clostridium difficile* infection were 73.80% of patients, the Relative Risk for second antibiotic treatment for this infection being 1.75630, P=0.0483. Of antibiotic therapy regimens quinolones and third generation cephalosporins are preferred, particularly in surgical ward and ICU. After updating elements for prevention in nosocomial infections with *Clostridium difficile*, at the end of 2013, a serious decrease was noted in the hospital starting with 2014.

Conclusions. *Clostridium difficile* infections in hospitals can be avoided by selective medical assistance of vulnerable patients due to their age and comorbidities, especially if they have personal history of recent antibiotic therapy.

Keywords: *Clostridium difficile*, Relative Risk, antibiotics

***ENTEROCOCCUS FAECALIS* AND *ENTEROCOCCUS FAECIUM* RESISTANT TO GLYCOPEPTIDES, PHENOTYPIC AND MOLECULAR CHARACTERIZATION**

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Introduction. Enterococci are part of the normal intestinal flora of humans and animals. *Enterococcus faecalis* and *Enterococcus faecium* are the most frequently enterococcal species isolated from human infections. Therapy of infections raises many serious problems due to intrinsic and acquired resistance to multiple antibiotics. The acquisition of resistance to glycopeptides affects the treatment and control of infection with this microorganisms and particular in cases of infections with *Enterococcus faecium*.

Material and Methods. We analyzed the antibiograms performed between 01.01.2008 - 31.07.2014 in terms of resistance to beta-lactams, aminoglycosides, quinolones and glycopeptides. We performed the MIC for glycopeptides by microdilution method, and in cases of glycopeptides - resistant strains we determined the presence of Van A and Van B genes.

Results. We analyzed 1254 strains of *Enterococcus faecalis* and we observed that 1.5% strains were resistant to vancomycin and 0.9% to teicoplanin. The 457 strains of *Enterococcus faecium* had 18.8% resistance to vancomycin and 3.4% resistance to teicoplanin. The first strains with resistance to vancomycin have appeared in 2010 (*Enterococcus faecium*) and 2011 (*Enterococcus faecalis*).

Conclusions. In our study the resistance profile differs between *Enterococcus* species. The species with the highest resistance was found to be *Enterococcus faecium* witch is resistant to many classes of antibiotics, namely beta-lactams, quinolones, aminoglycosides, glycopeptides and nitrofurantoin and the *Enterococcus faecalis* strains had a relatively low prevalence of resistance.

CURRENT PRACTICE IN THE TREATMENT OF *HELICOBACTER PYLORI* INFECTION

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Helicobacter pylori (HP) is one of the most common infections worldwide. Many studies proved its association with gastroduodenal ulcer, gastric adenocarcinoma, MALT gastric lymphomas and some forms of anemia. There are multiple pathogenic factors of HP: Vac A vacuolated cytotoxin, the urease, the lipopolysaccharide, stimulation or inhibition of acid secretion, induction of chronic inflammation of the gastric mucosa. The risk of disease is higher when some pathogenity factors of HP strains coexist with genetic polymorphisms of the host.

There are many treatment regimens recommended, but non of them provide satisfying eradication rates in the context of evolution of HP antibiotic resistance. The classic regimen, containing a proton pump inhibitor (PPI), associated with clarithromycin and amoxicilin or metronidazole for 7-14 days provided maximum eradication rates of 81-83%, but it decreased to 70% in the last few years. It has been observed that 14 days regimens provide higher eradication rates. Quadruple therapy associating bismuth salts, PPI, tetracycline and metronidazole is recommended as first choice regimen in the areas with high HP resistance to clarithromycin or as second line therapy, in case of therapeutic failure of triple therapy. Other therapy regimens are sequential therapy and the regimen with levofloxacin. Associating prebiotics or probiotics in order to reduce the adverse effects showed promising results..

In case of second line therapy failure it is necessary to test the sensibility of the HP strain to antibiotics. There are molecular biology techniques for testing HP susceptibility to clarithromycin and fluoroquinolones.

Keywords: *Helicobacter pylori*, pathogenity, treatment, resistance

PREVALENCE OF THE INFECTIONS CAUSED BY CAMPYLOBACTER SPP. AS ETIOLOGICAL AGENT IN DIARRHEAL DISEASES IN CHILDREN

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Background&Aims. Campylobacteriosis is a zoonotic infectious disease found in both emerging and developed countries, its main source being the farm animals (poultry, cattle, swine), but also house pets. It is estimated that the incidence of the disease is much higher than the official reports show, due to incorrect diagnosis and/ or underreporting.

This study aims to obtain information regarding the incidence of infections caused by Campylobacter spp. in diarrheal diseases in children, in two different areas of Romania (historical regions: Moldova – Iasi and Bacau Counties and Muntenia – Prahova, Arges, Ilfov Counties and Bucharest).

Patients and Methods. During the 1st of January, 2014 and the 30th of June, 2014, a number of 290 pathological specimens were tested for Campylobacter spp antigen determination in Synevo Clinical Laboratories from Bucharest and Iasi. The samples were collected in sterile containers, without conservation media, using refrigerated delivery. Tests were performed in the same day the specimens were collected, using the immunoenzymatic method (CerTest, BIOTEC) confirmed by direct microscopy, Gram coloration, examination with an immersion objective (1000x).

Results and Discussion. 62 out of 290 tested specimens were positive (21.38% of the total number of collected samples). The percentage of positive results was split by age groups, as follows: 41,93% - children between 1-2 years of age, 22.58% - children under 1 year, 11.29% - children between 2-3 years and 4-5 years of age, 9.68% - children between 5-11 years and only 3.23% - children between 3-4 years.

The distribution of positive results between the two historical areas of the country is similar, both presenting a maximum incidence for the 1-2 years of age group.

Conclusions.

1. The study shows the prevalence of this type of infectious disease in neonates and small children, which is an important finding given both the heavy symptoms and the potential late complications (Guillain Barre syndrome) in the absence of adequate treatment.

2. Microbiology Labs have the important role to diagnose (in a right and fast manner) this type of infection because of the diverse treatment schemes (compared to other bacterial etiologies of the acute diarrheal diseases).

3. Subsequent long term studies are necessary in order to assess the epidemiologic aspects of this type of zoonosis in our country.

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CORRELATION BETWEEN INFECTIONS OF THE BILIARY TRACT AND INTRA- AND EXTRAHEPATIC BILIARY MALIGNANCIES

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Background and Aims. Bile duct tumors are rare and have related risk factors with sclerosing cholangitis in ulcerative colitis, parasitic and viral infections, hepatolithiasis, occupational exposures to arsenic and thorium dioxide/radiology. The objective of this paper is to establish cluster distribution of two morbid entities, starting from the assumption that distribution is uneven for both morbid entities in Arad county, being present in the same areas, and there is a correlation between them, with determinism of certain intra-and extra-hepatic biliary ducts infectious in the development of malignancies at this level.

Material and method. We analyzed by Besag & Newell's Method, geospatial distribution of prevalence for biliary malignancies as rare disease versus incidence for acute and chronic infections of intra-extrahepatic biliary as common disease. Distribution was obtained with the ClusterSeer, Besag & Newell method, which have been set for different cut-off values of k.

Results. Between July 2013-June 2014 were assisted in Arad infectious diseases unit 67 of angiocolitis, cholecystitis, acute and chronic lithiasis and/non lithiasis cases, which were compared with geospatial distribution of bile duct tumors or Arad County, recorded cases between 1993-2013, 422 in total. Biliary infections formed a cluster with cut-off k34, $P=0.040$, two clusters k35, $P=0.045$, six clusters k36, $P=0.029$, eight clusters k37-38, $P=0.020$ and ten clusters k39, $P=0.017$, which were found overlapping distribution for the biliary tract malignancies: a cluster k145, $P=0.037$, two clusters k150, $P=0.045$, seven clusters k160, $P=0.010$, nine clusters k170, $P=0.006$, for the same locations, all in the south-western part of Arad County, sharply delimited. Both samples are representative for Arad county population to a confidence level of 95% CI and 3.08 margin of error. The correlation for biliary infections with bile duct malignancies is positive 0.987506.

Conclusions. Determinants for bile duct tumors are multifactorial, acute and chronic infections are shown to be strongly involved for some entities. Rare biliary cancers in Arad have an uneven geospatial distribution which is reflected in the distribution of clinically symptomatic biliary tract infections, these patients being candidates for cancer at this level. Management of such patients must take into account this demonstrated correlation between infectious disease and cancer.

Keywords: Besag & Newell's Method, cluster, infections, malignancies

TOXOPLASMA ENCEPHALITIS IN HIV INFECTED PATIENTS

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Background: Toxoplasma encephalitis (TE) is one of the most severe neurological infection encountered in HIV infected patients (PIH); after the introduction of the combined antiretroviral treatment (ART) the prevalence of TE dropped down, however this illness remains an important cause of morbidity and mortality in PIH.

Objectives of the study: to evaluate prevalence and evolution of TE in PIH under ART.

Material and method: retrospective study (01 January 2004 – 31 December 2013) including 728 PIH under monitoring of the Regional Center for Monitoring and Evaluating HIV/AIDS Infection, Craiova; we have evaluated clinical data, head CT scans results, the presence of anti *Toxoplasma gondii* antibodies, immunological and virological data, as well as ART history of the PIH.

Results: The prevalence of TE for the studied group of PIH was 4.3% (34/728); characteristics of the PIH with TE was as follows: mean age = 28.2 ± 11.2 years, diagnosis of AIDS (clinical and/or immunological) prior to the diagnosis of TE = 30 PIH (88.2%), average ART regimens = 4.1 ± 2.1 , average CD4 count = 70 cells/mm³ [2, 210]. Clinical manifestations has been dominated by headache – 29 PIH (85.3%), altered consciousness – 23 PIH (67.6%), focal neurological signs – 11 PIH (32.4%); the most common CT appearance was represented by annular lesions in the brain – 25 PIH (76.5%). Death rate was 29.4% (10/34), factors associated with death being: CD4 count < 50 cells/mm³ (p=.0009), presence of coma (p=.002), presence of focal neurological signs (p=.004), low adherence to ART and to the primary prophylaxis of TE (p=.002).

Conclusions: TE is one of the opportunistic infection potentially severe in PIH; a good adherence to ART and to the primary prophylaxis could lower the prevalence of TE.

Keywords: encephalitis, toxoplasmosis, HIV

PROGNOSTIC FACTORS IN THE EVOLUTION OF HIV – TUBERCULOSIS CO-INFECTION

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Background: Human immunodeficiency virus (HIV) and Mycobacterium tuberculosis infections are frequent associated, even in the era of highly active antiretroviral therapy (HAART), generating a negative effect upon patients' evolution and prognosis.

Aim: to identify and assess factors influencing the evolution and prognosis of HIV – tuberculosis (TB) co-infection.

Patients and methods: We performed a retrospective, analytical study, over a 5-years time interval (June 2009 – June 2014), by comparing two categories of HIV-infected patients: with TB and without TB, from the point of view of demographic data, history of HIV infection, immune and viral status, TB diagnosis, resistance to anti-TB medication and death rate.

Results: Within the above-mentioned 5-year period, 444 HIV-positive patients were monitored in the Regional anti-HIV/AIDS Fight Center Mureș, out of which 328 under HAART. TB was diagnosed in 79 patients (17,79%), out of which 28 were infected with multi-drug-resistant (MDR) and 2 with extensive-drug-resistant (XDR) strains of Mycobacterium tuberculosis. TB was associated with severe immune suppression (CD4+ T-cells level below 200 cells/μL) and high HIV-ARN plasma viral load (VL), over 100000 copies/mL. We registered 58 (13,06%) death among HIV-infected patients during the studied time period, out of which 28 (48,27%) caused by TB (18 MDR or XDR TB cases). We found a positive, statistically significant association between MDR/XDR TB and death ($p = 0,0009$, OR = 5,850, 95% CI = 2,134 – 16,3).

Discussion: HIV-TB co-infection has negative, synergistic impact upon the patients immune status, reducing life expectancy.

Conclusions: During HAART era, HIV-TB co-infection continues to represent one of the main causes of death in HIV-positive patients. The development of MDR and XDR strains of Mycobacterium tuberculosis represents a poor prognosis factor.

INFECTION WITH HUMAN IMMUNODEFICIENCY VIRUS - ANOTHER DISEASE WITH 1000 FACES

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Background & Aims. The number of HIV infected persons is rising, its detection relies on screening related to the symptoms suggestive for the immunodeficiency syndrome. The goal of this work is to note the cases detected and tracked in the department of supervision of HIV/AIDS infection in Tg.Mureș, in the year 2014.

Patients and methods. The retrospective transversal study consisting of 16 patients detected with HIV and kept on the record by the department of supervision of HIV/AIDS infection in Tg.Mureș in the first 7 months of the year 2014. The demographic data, motives of testing, stage of disease, immune status were tracked and observed.

Results. From the 16 patients, 11 male and 5 female, the average age was 33 (the extremes are 13 and 54) . 6 patients were detected because of diseases that suggested immunodeficiency, like cerebral toxoplasmosis, wasting syndrome associated with pancytopenia, diarrheic disease lasting more than a month, pulmonary tuberculosis. 4 patients were tested because of sexual exposure, 2 with recently diagnosed partners, 2 who were living with known HIV patients. 6 have been detected through screening for pregnancy, blood donation, accidental exposure to biologic material at the workplace, recipient for stem cells, 2 with sexual activity with high risks. The transmission for 13 patients was sexual, at 2 patients it was possibly parenteral (belonging to romanian cohort, late presenters) , one unknown case (13 year old patient with pulmonary tuberculosis). The clinical-immunological status at the moment of the report: A2:5, B1:2, B3:1, C1:1, C3:4. Level of TCD4 limfocytes was 489/μl (minimum 11 μl, maximum 2170 μl). Discussion: The number of newly diagnosed patients is on the rising with the modification of the epidemiologic character.

Conclusions. The detected patients were mostly male, the average age was above the national cohort, the route of transmission was predominantly sexual, the main cause of testing was the screening, only 5 were in the AIDS stage, the average level of TCD4 limfocytes was 489/μl. The polymorph manifestation, the variety of the motives for the disease underlines the importance of HIV screening in different specialties.

Acknowledgement to all the colleagues and patients who have contributed to this work.

RHODOCOCCLUS INFECTION IN A SEVERE IMMUNOCOMPROMISED HOST. CASE PRESENTATION

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Background. Rhodococcus spp. causes a zoonosis, and rarely affects human host, especially immunocompromised host. The most frequently encountered manifestation is necrotic pneumonia that can be associated with extra pulmonary manifestations. There are two pathogenic species of Rhodococcus *facians* and *equi*. Rhodococcus is a Gram positive bacillus, sometimes acid fast, belonging to the order of Actinomycetes, and can be mistaken for Mycobacterium spp, Nocardia(NC) or saprophytic Corynebacteria. In HIV-Rhodococcus co-infected patients the mortality was up to 60% in the pre HAART era.

Aims. Report of clinical, haematological, bacteriological, radiological, immunological aspects and response to treatment of a HIV+ patient infected with Rhodococcus equi.

Method - retrospective study

Results. A young 36 year old man, admitted for fever, cough, fatigue, weight loss, after an evolution of 30 days . He is treated for pyo-pneumothorax in the surgery department with a chest tube. The thoracic CT scan showed a necrotic pseudotumor, and multiple alveolar foci in the upper right lobe. Search of sputum and pleural fluid showed acid fast bacilli, coccoid forms, the cultures being positive for NC. Rhodococcus spp was identified by biochemical characteristics (API tests). Serologic tests for HIV were positive, the patient being a very late heterosexual presenter for HIV infection with 10 CD4/mm³ and a viral load log₁₀ 5.41copies/ml. He received a multiple drug regimen with Biseptol, iv Aminoglicosides and Carbapenems for 40 days, and then Claritromicine, Biseptol and Ciprofloxacin, 2 month orally. After 6 weeks of evolution with severe symptoms-meningeal syndrome, respiratory insufficiency, diarrhoea, the patient received HIV treatment and he had a favourable outcome.

Conclusion. Rhodococcus is a rare opportunistic infection in HIV, and should be considered in the differential diagnostic of a necrotic pneumonia and a systemic infection in HIV infected persons. There is no standardised treatment, but it seems that an associated antibiotherapy favours a better prognosis. A multidisciplinary work team (surgical and medical) may be requested.

HIV POSITIVE PATIENT WITH PSORIASIS AND SEPSIS DUE TO STAPHYLOCOCCUS LUGDUNENSIS – CASE PRESENTATION

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BRÎNDUȘA ȚILEA, NINA ȘINCU

Background & Aims. *Staphylococcus lugdunensis* is a coagulase-negative *Staphylococcus*, part of the normal flora of the skin, however its virulence resembles that of *Staphylococcus aureus*, since it can produce skin, soft tissue, joint and bone infections, endocarditis, sepsis, staphylococcal toxic shock syndrome, catheter related infections. The majority of the strains are sensitive to Oxacilin, quinolones, Trimethoprim-sulfamethoxazole, aminoglycosides, all of the strains are sensitive to Vancomycin. The aim of this paper is to present the case of an HIV positive patient with psoriatic erythroderma and sepsis with *Staphylococcus lugdunensis*.

Patients and methods. The case of a 28 years old male patient is presented, known HIV positive and with psoriasis, non-adherent to the antiretroviral therapy, with T CD4 + lymphocyte count of 4 cells/mm³, admitted for fever, chills, weight loss, cough, with generalized erythema and desquamation of the skin, conjunctivitis. The white blood cell count was 7790 cells/mm³, with 88.5% of neutrophils. A bacterial or an opportunistic infection, or fever due to psoriatic erythroderma was suspected. Ceftriaxon and Ciprofloxacin were administered. The outcome was unfavorable, with low blood pressure (70/40 mmHg), oligoanuria, tachycardia, altered status. Vancomycin and Fluconazole were added, intravenous fluid replacement and local steroid therapy was given, and the patient's status improved.

Results. *Staphylococcus lugdunensis* was cultivated from two separate blood culture samples. The antibiotic therapy was modified according to the sensitivity test to Ciprofloxacin, Clindamycin with Gentamycin, and the outcome was favorable.

Discussion. *Staphylococcus lugdunensis* could be interpreted as a contaminant coagulase-negative *Staphylococcus*, and therefore ignored in the clinical practice, although it behaves like *Staphylococcus aureus*. Its identification was very helpful in the management of the case presented.

Conclusions. The blood culture samples containing *Staphylococcus lugdunensis* should not be considered as contaminated, they should be analyzed taking into account the clinical data, especially in case of patients with immunodeficiency.

Acknowledgement. we are thankful to the laboratory staff (Előd Nagy, Grațiela Tripon, Camelia Vintilă) for the isolation and identification of *Staphylococcus lugdunensis*.

IS FERRITIN AN ALLY OR AN ENEMY OF THE RHEUMATOLOGIST'S ARSENAL?

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Ferritin is a major iron storage protein involved in the regulation of iron availability. Thus, it is a valuable tool for both for the evaluation of common disease states, such as iron-deficiency anemia, and for evaluation of hereditary and acquired iron-overload conditions, such as hereditary hemochromatosis and chronic transfusion therapy. Ferritin is also an acute-phase protein and marker of acute and chronic inflammation. Its expression is up-regulated in conditions such as infectious, cancer and inflammatory processes. Very high serum ferritin levels are a diagnostic clue of two clinical entities, hemophagocytic syndrome and Still's disease.

Serum ferritin, as dual role molecule used in the diagnostic process of human diseases will be reviewed in this paper from the rheumatologist's point of view.

THE IMPLICATIONS OF OBESITY IN IMMUNITY, INFLAMMATION AND INFECTION

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Adipose tissue is no longer considered an inert energy storage organ, but a highly active endocrine and metabolically important organ. By secreting an array of signaling molecules, termed adipokines, communicates with and influences other organs and systems including brain, liver, muscle, bone, endocrine, reproductive and immune systems and adipose tissue itself. Being an important source of several hormones, cytokines, chemokines, growth factors and complement proteins, adipose tissue plays an important role in energy balance, insulin action, lipid and glucose metabolism, angiogenesis and vascular remodeling, blood pressure, coagulation, bone metabolism, inflammation and immunity. Obesity disturbs adipokines and induces a broad range of disorders, including metabolically, cardiovascular, endocrine, tumoral, inflammatory and immune. Obesity also induces chronic low grade inflammation by down regulation of anti-inflammatory adipokines, and increased levels of pro-inflammatory adipokines, tumor necrosis factor (TNF- α), monocyte chemo-attractant protein (MCP)-1 and interleukin (IL)-6. Adipose tissue is deeply implicated in immunity, being considered an ancestral immune organ. Adipocytes share with a diverse set of immune cells (including T cells, macrophages, and dendritic cells) several features, such as complement activation, production of inflammatory mediators to pathogen sensing and phagocytic properties. Obesity has been shown to affect leucocyte chemotaxis, natural killer cell functions, impair macrophage differentiation, affect cytokine production, and cause imbalanced cross-talk between the immune system and adipose cells. Obesity is related to several diseases that have been shown to affect the immune system and wound-healing including type 2 diabetes, cancer and vascular diseases, having also a significant impact on the respiratory system and lung immunity. Thus, obese patients have an increased susceptibility to infections with a number of different pathogens such as community-acquired tuberculosis, influenza, Mycobacterium tuberculosis, coxsackie virus and Helicobacter pylori. During the 2009 H1N1 influenza pandemic, obesity was identified as an independent risk factor for multiple markers of disease severity. Several studies indicate that obesity is a patient-related risk factor for nosocomial infections. Nowadays obesity pandemic and its many implications in multiple systems disorders place obesity as a major burden on health services.

Keywords: obesity, adipokines, inflammation, immunity, infection.

REACTIVE ARTHRITIS: PATHOGENESIS AND CLINICAL CONSIDERATIONS

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Reactive arthritis (ReA), a member of the spondyloarthritis group, was traditionally defined as an aseptic inflammatory arthritis triggered by a distant infection. In genetically predisposed individuals, infections with arthritogenic pathogens may trigger an immune reaction. Human leucocyte antigen (HLA)-B27 is the best known predisposing factor for ReA. The causative pathogens include *Chlamydia trachomatis*, *Ureaplasma*, *Yersinia*, *Shigella*, *Salmonella* and *Campylobacter*. Recently, using more sensitive techniques including immunohistology, electron microscopy and polymerase chain reaction (PCR), it was shown that bacterial components may persist into the joint. Currently, ReA is better defined as an immune-mediated arthritis, triggered by a bacterial infection, with no cultivable microbes in the joint, but showing intra-articular persistence of viable bacteria and/or immunogenetic bacterial antigens.

There are no universally accepted classification or diagnostic criteria for ReA. The diagnosis is mainly clinical, based on asymmetric oligoarthritis of the large joints that occurs within 2-4 weeks after a gastrointestinal or genitourinary infection. Other musculoskeletal manifestations include enthesitis, dactylitis and sacroiliitis/spondylitis. Patients with ReA may also have urethritis, cervicitis, conjunctivitis, uveitis, circinate balanitis, keratoderma blenorrhagica and onycholysis. The characteristic clinical triad of arthritis, urethritis and conjunctivitis, formerly known as Reiter syndrome, is a subset of ReA. No laboratory or imaging finding is diagnostic of ReA.

Treatment of ReA is mostly symptomatic with nonsteroidal antiinflammatory drugs and topical corticosteroids. Limited evidence exists about the use of conventional disease modifying anti-rheumatic drugs (DMARDs) and anti-TNF α agents. The use of antibiotics in ReA remains controversial.

THE SEPSIS CHALLENGE

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Sepsis (defined according with ACCP/SCCM recommendations) is an important challenge for clinicians and researchers because of high mortality (15-50%) and incompletely understood pathogenesis.

The host innate immune response in sepsis depends on the microbial load or virulence and host factors (age, comorbidity, genetic factors) and is characterized by pro-inflammatory and anti-inflammatory mechanisms that appear simultaneously.

These dynamic mechanisms are activated by the release of cytokines, chemokines and other inflammatory regulators as a response to cellular injuries.

Pro-inflammatory phase (release of pro-inflammatory cytokines: TNF alpha, IL-1, IL-6, IL-8, IL-12, IFN-gamma) evolve with hyper-inflammation that lead to endothelial dysfunction, vasodilatation, hypotension and finally organ dysfunction.

Anti-inflammatory mechanism (release of anti-inflammatory cytokines: IL-1-Ra, IL-4, IL-10, IL-13, TGF-beta) are associated with immunosuppression state and immunoparalysis which play a central role in inducing infections with resistant germs, tissue damage, multiple organ failure and finally death.

Early diagnosis of sepsis is vital for reducing mortality and can be done by increase awareness of the physician and by establishing a multi-marker panel that include pro-inflammatory and anti-inflammatory biomarkers.

In present the main treatment for sepsis is supportive. Future sepsis treatment are immunomodulating strategies, even that clinical trials performed were unsuccessful (administration of anti-TNF-alpha and anti-IL1). Further research is necessary.

MECHANISMS OF INFLAMMATION AND THE ROLE OF CYTOKINES IN THE PATHOPHYSIOLOGY OF ACUTE MENINGITIS

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Acute meningitis is a serious disease, characterized by inflammation of the meninges (pia mater and arachnoid). Despite early and adequate treatment, meningitis still results in significant mortality, mostly in children and elderly. Furthermore, recovery is often associated with persistence of serious sequelae.

The pathophysiology of viral, bacterial and fungal meningitis is still poorly understood. Brain damage after infection of the meninges may be induced directly by the infectious agent or may be the effect of the inflammatory host response to the infection. Leukocytes, macrophages/ monocytes, microglia release free radicals, proteases, cytokines, finally leading to energy failure and cell death.

Nowadays, there is a constant interest in studying the inflammatory response and production of cytokines in the cerebrospinal fluid of patients with bacterial and viral meningitis. Conversely, there are few reviews about this aspects regarding tuberculous and fungal meningitis.

The purpose of this presentation is to summarize current knowledge about the mechanisms of inflammation and the roles of pro- and anti-inflammatory cytokines during acute viral, bacterial and fungal meningitis.

Keywords: meningitis, inflammation, cytokines pro- and anti-inflammatory, cerebrospinal fluid.

MANAGEMENT OF HEPATITIS B AND C VIRUSES REACTIVATION IN PATIENTS UNDER IMMUNOSUPPRESSIVE THERAPIES

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In the last decades the number of patients under different immunosuppressive therapies (chemotherapy, corticotherapy, monoclonal antibodies, anti-TNF etc.) has significantly increased. In these patients the rate of mortality due to hepatic impairment is more than 5%, often due to HBV reactivation.

HBV reactivation may occur in 20-50% of patients under immunosuppressive treatment or chemotherapy for different malignancies. Immunosuppression leads to loss of immunity for HBV infection. After chemotherapy/immunosuppressive treatment is discontinued and the immune response is recovered, the immune activity against HBV is reinstated, which leads to a masive lysis of infected hepatocytes, often leading to fulminant hepatitis with a mortality rate up to 40%. HBV reactivation can occur in case of immunosuppression, including patients with aparently cured HBV infection(occult HBV infection) or with inactive HBV infection. In patients with organ transplant, in which immune recovery is not possible, high viral loads are associated with occurrence of fibrosing cholestatic hepatitis caused by the direct cytopathic effect of HBV. For these reasons, European and American therapeutic guideliness recommend determining HBs Ag, HBs Ab and IgG HBc Ab in all patients that will start an immunosuppressive treatment.

Chemotherapic regimens used in hematologic malignancies treatments are frequently associated with HBV reactivation, especially those with monoclonal antibodies. Intraarterial chemoembolisation and therapies with antitumoral necrosis factor can also be associated with HBV reactivation. Additional risk factors for HBV reactivation during immunosuppressive treatments are male gender, high viral load prior to chemotherapy initiation and the diagnose of malignant lymphoma or breast cancer.

In patients with positive HBs Ag and low viral load, preemptive antiviral treatment should start with one week prior immunosuppressive treatment initiation and continued for 6-12 months after the end of immunosuppressive therapy. For patients with high viral load, antiviral treatment is continued until reaching the end-points establised for immunocompetent patients with HBV infection.

In patients with negative HBs Ag, preemptive antiviral treatment is not necessary, but transaminases and viral load must be monitored considering the possibility of occult HBV infection reactivation with retroseronversion in HBs system (disappearance of HBs Ab and recurrence of HBsAg).

Keywords: viral hepatitis, reactivation, immunosuppressive therapy

PRO AND ANTI-INFLAMMATORY SERUM CYTOKINE PROFILE IN ACUTE VIRAL HEPATITIS B IN ADULTS

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Background. Hepatitis B virus infection may produce a wide spectrum of clinical illnesses, from asymptomatic infection to limited acute hepatitis, fulminant hepatitis with acute liver failure, chronic hepatitis, cirrhosis and hepatocarcinoma. These different outcomes rely on viral factors and host immune response. The balance in cytokine production profiles may play a crucial role in inducing the persistence or resolution of hepatitis B viral infection.

Objectives: To analyze the cytokine's profile in adult patients with non-fulminant acute hepatitis B versus a control group, to reveal the differences between the cytokine's serum concentrations and HBe Ag status at admittance. Another aim was to analyze the correlations between the cytokines levels and the biochemical parameters at admittance.

Methods. The serum levels of interleukin IL-1Ra, IL-10, IL-6 and IL-1beta were determined by multiplex xMAP technology (Luminex) in 36 adult patients with non-fulminant acute hepatitis B admitted over a 3 years period and 14 healthy volunteers.

Results. The serum concentration of IL-1Ra and IL-10 were significantly higher ($p < 0.05$) in hepatitis B patients than in the healthy volunteers. We did not found statistically significant differences for IL-6 ($p = 0.88$) and IL-1beta ($p = 0.50$) between the hepatitis B subjects and the control group. The four cytokine serum levels did not differ ($p > 0.05$) between the patients with acute hepatitis B with HBe antigen versus those without HBe antigen at admittance. The serum level of IL-1Ra was positively correlated ($p < 0.05$) with IL-10 ($r = 0.61$) and IL-6 ($r = 0.40$). The level of IL-6 was positively correlated ($p < 0.05$) with IL-1beta ($r = 0.34$). IL-1Ra proved a negative correlation with ALAT ($r = 0.32$, $p < 0.05$). The serum concentration of IL-6 showed a positive correlation with bilirubin serum levels ($r = 0.40$, $p = 0.01$). The present study proved that the serum level of IL-10 higher than 1.7 pg/ml correlated with the absence of HBs antigen at 6 months of follow-up ($p = 0.007$, OR 19.24, 95%CI=1.03-373.3).

Conclusion. The study proved that non-fulminant acute hepatitis B patients recorded higher levels of IL-1Ra and IL-10 compared with controls. None of the four studied cytokines recorded significant differences in relation to the HBeAg status at admittance. IL-10 higher than 1.7 pg/ml correlated with the absence of HBsAg at 6 months.

Keywords: cytokines, non-fulminant hepatitis B, IL-1Ra, IL-10.

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RISK OF INFECTION IN PATIENTS WITH INFLAMMATORY RHEUMATIC DISEASES TREATED WITH IMMUNOSUPPRESSIVE THERAPY

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Rheumatic diseases are associated with a number of immunological alterations and may themselves predispose to infections. Several studies have reported an increased risk of infection in patients with rheumatic diseases compared to general population (1).

Therapy with glucocorticoids (GCs), conventional disease-modifying anti-rheumatic drugs (DMARDs) and biological agents can play an additional role in increasing this risk. In addition to the actions of these drugs, their dose and the duration of treatment, there are other factors that contribute to the development of these adverse outcomes like: the nature of the underlying disease process, the functional status and medical fragility of the patient, the concomitant use of other immunosuppressive medications (2).

The risk of infection increases with the dose of GCs and duration of treatment and tends to remain low in patients exposed to low doses, even if the cumulative dose is high (3). The results of five trials which involved patients with rheumatic diseases showed no increased relative risk. The use of the lowest possible GC dose, at night, and for the shortest possible time should greatly reduce the risk of infections (4).

The most frequent infections associated with methotrexate (MTX) involved the skin and upper respiratory tract, but there was no increase in serious infections leading to drug withdrawal. It was reported a relationship between the risk of pneumonia and leflunomide use in RA, whilst no increased risk was found with sulphasalazine or MTX (5).

The results regarding the risk of infections secondary to biological therapy are controversial. German biologics register (RABBIT) identified a trend for increased rates of herpes zoster (shingles) infection with TNF inhibitors (TNFi) compared with traditional DMARDs (6). Although there is no head-to-head comparison of the anti-TNF agents with regard to infection risk, recent observational data from Dutch RA registry have identified a trend for lower risk of infection for etanercept than with infliximab or adalimumab (7). Pneumocystis and mycobacterial infections accounted for almost half of the opportunistic infections occurring among new users of TNFi and most occurred within 6 months of TNFi initiation (8).

The risk of infection appears to vary between different types of inflammatory arthritis and different immunosuppressive agents. The physicians should anticipate this risk due to both usual and unusual organisms, and keep in mind that specific therapy may blunt classic clinical features and delay the diagnosis of this complication.

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ESTIMATES OF POPULATIONAL IMPACT OF INFECTION-ASSOCIATED CANCERS IN CLUJ COUNTY (2006-2010) AND PREVENTION IMPLICATIONS

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Introduction: In recent years, 11 infectious agents have been identified as causative factors of cancer in humans by the International Agency for Research on Cancer (IARC) in Lyon. In developing countries, the proportion of cancers attributable to infections (26%) remains about three times higher compared to industrialized countries (8%). In the last decade, in the Cluj County, the incidence of gastric, liver cancer and non-Hodgkin lymphoma showed an increasing trend in both genders, while a slight decrease in the incidence of cervical cancer was observed.

Objective: To estimate the population attributable fraction of infection-associated malignancies in the population of the Cluj County during 2006-2010 as a prerequisite for a better preventive approach.

Material and methods: The reported incident cases of cancer in the Cluj County were taken from the North-Western Regional Cancer Registry. The number of cancer cases attributed to each infection was calculated by multiplying the incident cases with the population attributable fraction (PAF%) by using specific local exposure prevalence for certain infectious agents and the estimated relative risk between each exposure and the associated cancer (literature data).

Results: The estimated number of cancers attributable to infections was 2,196 cases, representing 15.12% of all cancer cases. Population attributable fraction was - 6.60% for human papilloma viruses (HPV), 4.18% for *Helicobacter pylori* (Hp) and 3.8% for hepatitis B and C viruses, amounting to 96.45% (2118) of all cases with predominant localizations in the cervix, stomach and liver. Among the less common causes of cancer we found Epstein-Barr virus (EBV) with a PAF of 0.52% (76 cases), human herpes virus type 8 (HHV8) (1 case of HIV infection and Kaposi's sarcoma) and human lymphotropic virus with T cell type 1 (HTLV1) (1 case). Among all cases of infection-associated cancers, 1405 (20.44%) were identified in women and 791 cases (10.33%) in men. Cervical cancer accounted for 64.8% of all infection-associated cancers in women, followed by cancer of the liver (17.86%) and gastric cancer (14.66%). In men, gastric and liver cancers were dominant accounting for 87.74% of all cases (48.17% and 39.57%, respectively).

Conclusions: Our findings represent the first systematic assessment of infection-associated cancers in the Cluj County highlighting the burden of disease in women. From the public health perspective, the primary, secondary and tertiary preventive measures should be outlined, mainly for infections caused by HPV, Hp and hepatitis viruses.

Keywords: Cancer, causative factors, infectious agents, primary, secondary prevention

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STREPTOCOCCAL TOXIC SHOCK SYNDROME - CASE SERIES AND LITERATURE REVIEW

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Introduction: Streptococcal toxic-shock syndrome (STSS) is associated with invasive or noninvasive group A *Streptococcus pyogenes* infection. Global incidence is on rise in the last two decades and fatality rate remains high, 19-44%. Epidemiological surveillance includes characterization by T and *emm* typing, the presence of superantigen and other virulence coding genes. According to Strep-Euro Surveillance Program 2002-2004, STSS represents approximately 13% of confirmed severe streptococcal infections in Europe.

Objectives: Description of STSS cases diagnosed in the Teaching Hospital of Infectious Diseases Cluj-Napoca during 2007-2014 and a review of the literature in order to optimize the diagnosis, treatment and chemoprophylaxis for contacts.

Material and methods: Case identification was based on case definition (CDC 2010) and the literature review was done by searching the Medline and Web of Science 2000-2014.

Results: During 2007-2014 there were five cases of SSTS, aged 31-63 years, three were women. In two young women toxic shock was present at admission and no source of infection was identified in one case, for the other miscarriage sepsis was confirmed. Both have evolved dramatically with multiple organ dysfunction syndrome and meningo-encephalitis in the latter one. A 36-year man was found HIV infected coincidentally with STSS diagnosis of respiratory source and co-infection with *Mycoplasma pneumoniae*. All patients survived under clindamycin treatment and supportive measures (except for the case with meningo-encephalitis who received meropenem). The literature review identified relatively few cases but with a rising trend in recent years, affecting predominantly males and older groups of age with skin infection and diabetes mellitus. A prominent increase in young adults was observed in several countries. The annual incidence was 0.36 -3.17/100.000. The most frequently identified genotypes were *emm*1, 8, 81 and superantigen *speB* gene. In the absence of typical rash and skin source the diagnosis is difficult and the first line treatment of septic shock does not include clindamycin. Treatment with intravenous immunoglobulin associated to clindamycin seems effective (OR 0.12, 95% CL 0.01-1.29). The incidence of invasive disease in household contact of cases is thousands of times higher than in the general population suggesting the need of chemoprophylaxis in contacts. The limits of the studies were underreporting and small number of cases.

Conclusions: SSTS recognition is difficult and may be associated with inadequate treatment and poor prognosis. Better reporting is needed; treatment with clindamycin and immunoglobulin is beneficial and should be completed by chemoprophylaxis provided to contacts.

Keywords: Streptococcal Toxic Shock Syndrome, clindamycin, group A *Streptococcus pyogenes*

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FUNGAL MENINGOENCEPHALITIS IN AN IMMUNOCOMPETENT PATIENT CASE REPORT

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Fungal meningoencephalitis is the prerogative of immunocompromised patients. Cryptococcal meningoencephalitis rarely develops in immunocompetent subject, most often being an infection with *Cryptococcus gatti*.

The authors present the case of a man, of 46 years old, from rural area, several times hospitalized, developing optochiasmatic arachnoiditis, partial thrombosis of the cavernous sinus, polyuria-polydipsia syndrome within the slowly evolving, dragging on, meningoencephalitis, which turned to be cryptococcosis.

Laboratory data are presented (dynamics of the inflammatory syndrome, cerebrospinal fluid changes), the results of imaging investigations (excavated pulmonary nodules, occipital osteitis), treatment regimens followed (fluconazole, corticosteroids, dicumarol, mannitol). Investigations are reviewed in order to exclude a status of immunodeficiency (sternal puncture, HIV serology). Despite the late diagnosis, the evolution was favorable, including the follow up after one year.

Fungal meningoencephalitis should be part of the differential diagnosis of meningitis with clear CSF even in immunocompetent subject, treatment with fluconazole properly applied leads to a favorable outcome of the case.

Keywords: meningoencephalitis, *Cryptococcus gatti*, fluconazole

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RECCURENT INFECTIVE ENDOCARDITIS WITH STAPHYLOCCOCUS AUREUS IN A SEVERE SEPTIC CONTEXT, OCCURRED AFTER CORTISONE IMMUNOSUPPRESSION IN AN ADULT PATIENT WITH NASAL CARRIAGE OF STAPHYLOCCOCUS, CORRELATED WITH AN EARLY STAGE CHRONIC LYMPHATIC LEUKEMIA

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Background & Aims. The link between non-HIV immunosuppression and a possible former thundering infection without any severe potential (chronic nasal carriage of Staph).

Patient and methods. 53 years old patient, admitted in Rheumatology Clinic for lumbar pains with posterior irradiation in lower members which started 14 days before hospital admission. He was diagnosed with lumbago and received treatment with Diprophos for 10 days. Emphasized pains, Myalgia, polakiuria and sub fever were the reasons to address him to Neurosurgery Clinic. IRM-lumbar spine indicated acute septic arthritis L3-L4. The patient was admitted to the Infectious Disease Hospital Iasi with altered condition, fever (T-38,7C). Laboratory investigations reveal leukocytosis with lymphocytosis (WBC-49.500/mm³, Ly-52%), blood smear: some PMN with 'toxic granulations', chronic lymphatic leukemia aspect, positive inflammatory syndrome and the presence in nasal exudate, urine culture and blood culture of Staph. MSSA. The antibiotic treatment was according to the antibiogram. Day five, the patient suddenly presents dyspnea with orthopnea, aortic and left parasternal systolic souffle IV/6, high fever (T-39,2C), deteriorated condition and visual hallucinations. The echocardiography TT shows the possibility of an acute aortic regurgitation and valvular rupture by an infective endocarditis. During echocardiography TT, the patient developed phenoms of acute pulmonary edema and severe congestive heart failure, for which he remained in IBCV Iasi for 5 days, for antibiotic therapy and hemodynamic stabilization.

Results. When the patient came back to the Infectious Disease Hospital, blood culture revealed the presence of Staph. MRSA, reason to modify the antibiotic therapy with Vancomicine and Ciprofloxacin. He repeated the pulmonary edema crisis, using IOT and mechanic ventilation(for 95h). Urine culture reveals E.coli and P. aeruginosa and aspirate tracheobronchic culture reveals P.aeruginosa and Candida spp. (pneumonia associated with mechanic ventilation). The patient's condition maintained severe for one week, hemodynamically stable with positive inotrope support(dobutamine), decannulated day five (SaO₂-98%aa), with antibiotic therapy for another 14 days (Linesolid, Caspofungin), with good evolution. He returned at IBCV for cardiac surgery (mechanical prosthetic valve replacement of the aortic valve and mitral annuloplasty). Post-operative, the patient still presents leukocytosis with lymphocytosis, positive inflammatory syndrome, liverish cytolysis syndrome, reasons to ask for haematological consult (anisochromia, red blood cell aniso poikilocytosis, some dysplastic platelets, mature lymphocytes, Gumprecht nuclear shadows), which confirm the chronic lymphatic leukemia diagnose.

Discussion. After two years, the patient turned back to the Infectious disease Hospital with high fever (T-39,2 C), shivers, headache, precordial chest pains with anginous character, dyspnea, pronounced physical asthenia and right hypochondrium pain. We evidenced positive blood culture with Staph. MRSA and chronic nasal carriage. He received antibiotic treatment according to the antibiogram (diagnosis: infectious endocarditis with Staph. on a patient with prosthetic valve). The evolution was considered favourable.

Conclusions. Immunossuppressive treatment in patients with different chronic carriage (bacteria or virus) can cause specific evolution of acute infections with these etiologies, often with nefarious prognosis.

Keywords: reccurent infective endocarditis, cortisone immunosuppression, nasal carriage of Staphylococcus, chronic lymphatic leukemia

CHALLENGES IN THE DIAGNOSIS OF LYME NEUROBORRELIOSIS

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Background. *Borrelia burgdorferi* (Bb) sensu lato complex is responsible for an infectious disorder of the nervous system called Lyme neuroborreliosis (LNB), which represents a diagnostic challenge, due to the nonspecific manifestations, in addition to the low sensitivity of CSF culture and PCR for Bb.

The aim of our study was to draw attention on the risk of misdiagnosis of LNB.

Methods. retrospective, descriptive study of patients admitted to the National Institute for Infectious Diseases "Prof. Dr. Matei Bals" between 2008 and 2014. We included cases discharged with a diagnosis including at least one of the following: "Lyme", "neuroborreliosis" "burgdorferi".

Results. We included 43 patients, with median age of 40 years (min 20, max 68 years), 19 male. In 7 patients the LNB diagnosis was not confirmed. We found 36 patients in which diagnosis of certain LNB (11 patients) or possible/probable LNB (25 patients) was retained on discharge. In two cases the diagnosis of LNB was associated with multiple sclerosis diagnosis. Lumbar puncture was performed in 26 patients (4/7 unconfirmed cases and 22/36 confirmed cases). It showed pleocytosis (> 5 elements in 8 cases). Bb-specific antibodies produced intrathecally was proven in one of the three patients in whom it has been searched. In addition, the presence of IgG antibodies in CSF was demonstrated (Western blot) in another four patients, but without proving intrathecal specific antibodies synthesis. On the other hand, three patients have been labeled as having LNB despite the negative IgG immunoblot confirmatory test in serum. Antimicrobial treatment was administered in 26 patients (22 ceftriaxone, 3 ceftriaxone plus doxycycline and 1 doxycycline). We describe a fully documented case of LNB consisting of meningo-radicularitis with CSF pleocytosis of 38 elements/mm³, protein level of 281 mg/dl and Bb-specific antibodies produced intrathecally. The patient was successfully treated with ceftriaxone (for 28 days), followed by doxycycline (for 21 days) and both clinical manifestations and CSF changes disappeared after 8 weeks.

Conclusions. LNB is a relatively rare and treatable CNS disorder. For a better diagnosis accuracy of LNB (except for late LNB, which affects the peripheral nervous system), CSF exam should be performed, to look for the presence, but also for the intrathecal synthesis of Bb-specific antibodies.

EARLY DIAGNOSTIC BIOMARKERS IN LYME NEUROBORRELIOSIS – A CASE REPORT

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Background & Aims. Lyme neuro-borreliosis (LNB) is a nervous system infection caused by *Borrelia burgdorferi* sensu lato complex spirochaete, which is transmitted by arthropods belonging to the genus *Ixodes*. A variety of diagnostic biomarkers have been studied for a definite and early diagnosis of the disease, whereas the evolution and complications depend on the precocity of diagnosis and time of treatment initiation. Recent studies shows the presence of CXCL13 biomarker that can be revealed in the cerebrospinal fluid (CSF) immediately after infection, prior to specific IgM anti-Bb antibodies.

Case Report. We present the case of an urban patient aged 43, admitted with fever, headache, muscles and joints pain, and with the occurrence of peripheral facial paralysis. These symptoms emerged suddenly in the middle of apparent health, seven days prior to the admission. Epidemiological data revealed the fact that about 2 months prior to the onset of the present illness the patient was bit by a tick in Germany, his residential place. CSF examination revealed a clear liquid, with 280 cells/mm³ pleocytosis (60% lymphocytes, 40% granulocytes), 74mg/dl proteins and 48mg/dl glucose. CSF and serological tests (ELISA, Western blot) showed no anti-Bb IgM antibodies and revealed positive titres of anti-Bb IgG antibodies both in serum and CSF. The dynamics of CXCL13 chemokine in CSF was monitored. It presented values of 3800 pg/ml initially and 400 pg/ml after the treatment. The patient received 30 days intravenous treatment with 4 g ceftriaxone daily, followed by good evolution.

Conclusions. CXCL13 chemokine represents an early diagnosis biomarker for Lyme neuro-borreliosis, with a high sensitivity and specificity if uncertain serology.

Acknowledgement. The authors report no potential conflicts of interest

Keywords: neuro-borreliosis, biomarkers, diagnosis.

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LYME NEUROBORRELIOSIS – THE EXPERIENCE OF THE CLINIC OF INFECTIOUS DISEASES, CLUJ NAPOCA

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Aims: In the Clinic of Infectious Diseases, Cluj-Napoca, Romania, no study has been performed so far following the European diagnostic criteria for Lyme neuroborreliosis (LNB) that recommend cerebrospinal fluid (CSF) analysis. We have addressed the question if the apparent poor response to antibiotherapy is due to an incorrect diagnosis.

Patients and method: A prospective study included hospitalized patients with the suspicion of LNB between March 2011 - October 2012. Inclusion criteria: neurological symptoms, positive serology for *B. burgdorferi*, lumbar puncture, no previous parenteral antibiotherapy. A questionnaire was completed for each patient regarding previous or co-existing diseases, neurological, musculoskeletal, cutaneous, cardiac and ocular signs /symptoms at admission, end of treatment and 3 month later. Two negative binominal mixed effects regression models were used for statistical analysis. Two-tiered testing used an ELISA kit followed by a Western Blot kit and the intrathecal antibody index was calculated. Patients were treated as LNB with parenteral therapy for 21 days, indifferent of the CSF analysis results. Serological evaluation was repeated 3 month post treatment.

Results: Clinical, serological and cerebral MRI data of the patients will be presented. No case fulfilled the criteria for definite LNB, 7 cases were classified as possible LNB and in 33 cases LNB was invalidated. Statistical analysis showed a better response to therapy in the group of patients with possible LNB than in the group with LNB invalidated.

Conclusions: The study, that brings evidence that LNB is over diagnosed in our patients, is the first proof to stop antibiotics overuse in not confirmed LNB patients in our region. Our results confirm the statement that persistence of symptomatology after antibiotic therapy may be due to an incorrect diagnosis than to treatment failure.

Keywords: Lyme neuroborreliosis, Romania, intrathecal antibody index.

CLINICAL PARTICULARITIES AND MANAGEMENT OF TUBERCULOSIS DURING BIOLOGICAL THERAPY – THE INFECTIOUS DISEASES SPECIALIST POINT OF VIEW

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Tuberculosis represents a public health issue worldwide, WHO reporting over 2 billion infected people, most patients suffering from latent tuberculosis. Unfortunately, Romania is one of the countries with a high prevalence of both cases of active and latent tuberculosis. The use of biological therapies such as TNF-alpha inhibitors could cause the reactivation of latent infections, especially viral latent infections and tuberculosis.

The reactivation of latent tuberculosis in a patient under biological therapies is the main cause of therapy discontinuation, and also death. A great number of studies published in literature revealed an increased risk of tuberculosis reactivation in patients under biological therapies and, therefore, in most European countries, there are national registers for reporting these cases.

Of all the biological therapies currently available, the highest risk of tuberculosis reactivation is reported for TNF-alpha inhibitors (infliximab, adalimumab and certolizumab). This risk is lower for soluble TNF receptors (etanercept), anti CD20 antibodies or IL26-receptor inhibitors.

There are two essential issues regarding patients under biological therapy: the diagnosis of latent tuberculosis and the best method of prophylaxis for tuberculosis reactivation.

Therapeutic protocols in developed countries recommend chemoprophylaxis with isoniazid prior the biological therapy, for 6-9 months, with the possibility of initiating biological therapy after 2 months of isoniazid. Regarding the diagnosis of latent tuberculosis, most international guidelines consider susceptible for latent tuberculosis a person who lives in an endemic area of tuberculosis or who gets into contact with patients suffering from tuberculosis. Patients previously unexposed to tuberculosis are investigated with both tuberculin intradermic test and quantiferon TB gold or IGRA (interferon gamma release assay). If any of these tests is positive, the patient is diagnosed with latent tuberculosis.

Considering the fact that Romania is in the endemic area of tuberculosis, we might assume that all Romanian patients may be considered to have latent tuberculosis. Since 2010, Romanian guideline has required the performance of quantiferon TB gold before initiating the biological therapy. If this test is positive, the patient receives nine months of chemoprophylaxis with isoniazid. The biological therapy can be initiated after 2 months of isoniazid. Regarding the importance of chemoprophylaxis with isoniazid, numerous studies have shown that the relative risk of tuberculosis reactivation in patients without chemoprophylaxis is over four times higher than in patients who received chemoprophylaxis.

We think that it would also be useful for Romania to have a national register for patients with reactivation of tuberculosis during biological therapies for a better management of these patients.

DIAGNOSTIC VALUE OF FIBROBRONCHOSCOPY IN PULMONARY ASPERGILLOSIS

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Aspergillus speciae remain the most important opportunistic fungus for respiratory pathology in humans, in terms of frequency and diversity of clinical forms it produces.

Fibrobronchoscopy is an indispensable method for the diagnosis of any form of aspergillosis –cavitary, allergic or invasive.

Bronchoscopic techniques allow controlled sampling of cytological, mycological or pathological specimens, and all clinical guidelines appreciate it as essential to the diagnosis of opportunistic infections. Between these, bronchoalveolar lavage represents a relatively simple technique, which provides multiple ethio-pathogenetic information of the explored territory. In our practice we appreciate that it may frequently replaced transbronchial lung biopsy in diagnosis of diffuse infiltrative pulmonary lesions.

In our presentation we deal with theoretical aspects, but also the practical experience of the authors in the Clinical Hospital of Pneumology Cluj-Napoca.

Keywords: aspergillus, bronchopulmonary aspergillosis, fibrobronchoscopy

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MANAGEMENT OF TUBERCULOSIS DURING BIOLOGICAL THERAPY – EXPERIENCE OF THE THIRD DEPARTMENT OF “PROF. DR. MATEI BALS” NATIONAL INSTITUTE FOR INFECTIOUS DISEASES

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Background & Aims: Biological immunotherapy such as TNF-alpha inhibitors or anti-CD20 monoclonal antibodies revolutionized the treatment of autoimmune or hematological disorders. Unfortunately, patients receiving this therapy are at risk for reactivation of latent infections. The aim of this presentation is to analyze the characteristics of patients diagnosed with tuberculosis during biological therapy.

Patients & Methods: We present a series of 8 patients (5 women and 3 men) receiving biological therapy, admitted to Third Department of our hospital for prolonged fever. 7 patients received biological therapy for rheumatic diseases (rheumatoid arthritis, ankylosing spondylitis, psoriasis) and one patient for non-Hodgkin lymphoma. The patients received: Infliximab (3 patients), Adalimumab (1), Certolizumab (1), Etanercept (1), Rituximab (2).

Results: All patients were finally diagnosed with tuberculosis. The mean term of biologic therapy until the moment of diagnosis was 25.25 weeks. All patients had positive quantiferon-TB gold at admission. Bronchoscopy with bronchoalveolar lavage (BAL) was performed in all cases: one patient had AARB smear-positive in sputum and two patients had positive PCR for Mycobacterium tuberculosis from BAL. Only one patient was tested for latent tuberculosis before the initiation of biological therapy. All patients had a favorable outcome after classical anti-tuberculosis therapy (isoniazid, rifampicin, ethambutol, pyrazinamide).

Discussion: We have found in literature data that patients under biological therapy are at higher risk for bacterial and fungal infections and furthermore, for reactivation of latent viral infections and tuberculosis. We also registered an important number of cases of tuberculosis reactivation in our patients.

Conclusions: We emphasize the importance of anti-tuberculosis prophylaxis for patients diagnosed with latent tuberculosis, prior the onset of biological therapy. For Romania, a country with high incidence of tuberculosis, the diagnosis of latent forms and the prophylaxis with Isoniazid are even more important and might be necessary in all patients with autoimmune disorders who require biological therapy.

THE ROLE OF NON-ANTIBACTERIAL EFFECTS OF MACROLIDES IN THE CURRENT THERAPEUTIC APPROACH OF RESPIRATORY TRACT INFECTIONS

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Respiratory tract infections (RTI) represent a major public health problem around the world, associated with high morbidity and mortality, especially at extreme ages. In the last decades, the constant rise of pneumococcal resistance to antibiotics because of their excessive use led to higher mortality rates and difficulties in choosing the right treatment. Thus, in case of respiratory infections, antibiotic treatment must be prescribed exclusively in case of strong arguments for bacterial etiology. The chosen antibiotic for a RTI must cover a broad spectrum, active against the most common typical and atypical bacteria involved in RTI: *Streptococcus Pneumoniae*, *Haemophilus* spp, *Moraxella* sp, *Mycoplasma pneumoniae*, *Chlamydia pneumoniae* and *Legionella pneumophila*. The class of antibiotics with the most suitable spectrum for RTI and which concentrates very well in the respiratory tract is represented by macrolides (erythromycin, clarithromycin, azithromycin and josamycin). In contrast to other classes, macrolides have antiinflammatory, immunoregulatory and mucoregulatory effects, besides their antibiotic effect, which leads to better clinical and bacteriological success rates, compared to other classes of antibiotics. These nonantibiotic effects have been demonstrated in patients with chronic bronchitis exacerbations, mucoviscidosis and chronic sinusitis. The immunomodulatory and antiinflammatory effects proved to be beneficial in cases of flu complicated with bacterial superinfection, by significantly reducing the mortality rate compared to other classes of antibiotics. Current guidelines (IDSA/ATS-2007, BTS 2009, The Stanford Guide 2012) recommend macrolides and especially clarythromicin as a first choice antibiotic for low/medium-severity community acquired pneumonia, in patients without comorbidities or risk factors for resistance to antibiotics. Hospitalization is recommended in case of severe pneumonia, patients with comorbidities or with risk of antibiotics resistance. In these cases the first choice antibiotic treatment is either monotherapy with respiratory fluoroquinolone (moxifloxacin or levofloxacin), or association of a betalactamine with a macrolide (amoxicilin-clavulanate or ceftriaxone with clarithromycin).

Keywords: respiratory tract infections, macrolides, non-antibacterial effects

CARBAPENEMASE PRODUCING *KLEBSIELLA PNEUMONIAE* IN "DR. V. BABES" CLINICAL HOSPITAL OF INFECTIOUS AND TROPICAL DISEASES, IN 2013

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Objectives: isolation, identification and analysis of antibiotic resistance by phenotypic methods, confirmed by molecular methods, of *Klebsiella pneumoniae* strains involved in infectious processes, with different etiologic locations and extensive antibiotics resistance -by carbapenemase producing, in patients hospitalized in 2013, in "Dr. V. Babes " Infectious and Tropical Diseases Hospital (SVB).

Materials and Methods: Isolation and identification of *Klebsiella pneumoniae* strains was performed according to standard protocols (classic and automatic/VITEK2C), antibiotic resistance profiles were identified by standard disc diffusion method and MIC values by VITEK2C and E-test methods, according to CLSI 2013 Standard. Carbapenemase production was tested by screening methods: modified Hodge test (THM), E-test strips imipenem/imipenem + EDTA (IP/IPI/bioMerieux). Molecular confirmation was performed by RealTimePCR: *Klebsiella pneumoniae* DNA extraction was performed by "MasterPure™ Complete DNA and RNA Purification Kit" (Epicentre, Biotechnologies, Wisconsin), nucleic acids detection-quantification with "Primer Design™ Kit" (Primer Design 2X Precision MasterMix™ using specific primers for *blaOXA48*, *blaKPC*, *blaNDM*, *blaVIM*) and LightScanner 32 Instrument/LS32 (Idaho Technology, Salt Lake City, UT). Internal quality control: *E. coli* ATCC25922.

Results: 338 non-repetitive *Klebsiella Pneumoniae* strains were isolated and identified in 2013, in the Microbiology Laboratory of SVB, from a variety of biological samples. 42 *Kb. pneumoniae* strains (10/respiratory secretions, 18/urine cultures, 5/wound secretions, 9/other samples) (12.42%) were resistant to carbapenems, with positive THM. 5/42 strains *Kb. pneumoniae* THM (+), IP/IPI (-) were confirmed by RT-PCR as carrying *blaKPC* (*Klebsiella pneumoniae*-carbapenemase). 4/42 THM (+) strains IP/IPI (+) were detected *blaNDM* gene (New Delhi metallo-beta-lactamase). 6/42 strains THM (+) were confirmed for *blaOXA48* gene (oxacilinaza). No strain tested positive for *blaVIM* gene (Verona Integronics-encoded metallo-beta-lactamase). The remaining strains with positive phenotypic screening tests for potential production of carbapenemase will be subject to sequencing methods for detection of other coding genes. All *Kb. Pneumoniae* carbapenems resistant strains (carbapenemase producing) were sensitive to colistin; those isolated from urine cultures preserved their sensitivity to fosfomycin, while producing NDM strains were highly resistant to aminoglycosides.

Conclusions: The incidence of carbapenems resistant *Kb. pneumoniae* strains (carbapenemase producing) in SVB, in 2013, was 12.42% (5/*blaKPC* 4/*blaNDM*, 6/*blaOXA48*, 0/*blaVIM*). Polymyxins are the most common class of antibiotics used in treatment regimens, together with carbapenems, tigecycline, fosfomycin, aminoglycosides, etc., depending on resistance mechanisms identified in vitro.

Keywords: RealTimePCR, carbapenemases, KPC, metallo-beta-lactamase, NDM, OXA48

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THE EXPERIENCE OF ADULTS III DEPARTMENT OF MATEI BALS INSTITUTE IN THE MANAGEMENT OF HBV REACTIVATION IN PATIENTS UNDER IMMUNOSUPPRESSIVE TREATMENT

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Background. HBV infection remains an important public health problem worldwide despite the progress in the last few years regarding the efficiency and safety of antiviral therapies. HBV reactivation in patients under immunosuppressive treatment is associated with high rates of morbidity and mortality.

Methodology. We retrospectively analysed 5 cases of patients in evidence of Adults III department of Matei Bals Institute diagnosed with HBV reactivation due to immunosuppressive treatment.

Results. The case series included 3 males and 2 females, with a mean age of 44.2 years. Four patients were diagnosed with rheumatologic diseases (one patient with ankylosing spondylitis, two with rheumatoid polyarthritis and one with Reiter syndrome) and one patient with Non-Hodgkin Lymphoma. Of five patients, three received antiTNF α therapy and two received combined regimens (Prednisone+Cyclophosphamide+Rithuximab and respectively Methotrexate+Prednisone). Only one of them was screened for HBV and HCV infection before initiation of immunosuppressive therapy. All of them were hospitalized in Adults III Department of Matei Bals Institute in order to elucidate the cause of hepatic cytolysis that occurred during immunosuppressive treatment. Four patients had positive HBsAg with a titer median of 8270UI/ml [2.121-250.000 UI/ml]. One of them had negative HBsAg and a protective titer of HBsAb prior to initiation of immunosuppressive therapy; further on this patient developed HBs retroconversion, with disappearance of HBsAb and recurrence of HBsAg. All patients had negative HBeAg. Viral load median was 9log UI/ml[5.515-9.005 log UI/ml]. The median TGP value at admission was 934UI/L [348.5-1758.5 UI/L]and median of highest TGP value was 1720UI/L[834-2275 UI/L]. Median hospitalisation period was 27 days and it was significantly correlated with highest TGP values (p=0,0037)and it was not influenced by age or immunosuppressive regimen. In all patients antiviral therapy was initiated with entecavir. One of them had died due to hematologic disease.

Conclusions. Due to high risk of reactivation and its dramatic consequences, HBV infection screening is mandatory for patients diagnosed with malignant/autoimmune conditions that are due to receive immunosuppressive treatment. Preemptive antiviral therapy with potent nucleosidic analogues (entecavir, tenofovir) is recommended for all patients with HBV infection undergoing immunosuppressive treatments.

Keywords: HBV, reactivation, immunosuppressive treatment

CRITICALLY ILL PATIENTS FROM THE ICU OF THE TEACHING HOSPITAL OF INFECTIOUS DISEASES CLUJ-NAPOCA

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Background. In the ICU of the Teaching Hospital of Infectious Diseases Cluj-Napoca are treated patients with a complex pathology.

Aim. The main objective of this study was to identify the most frequent pathologies admitted to our ICU.

Material and Methods: This is a retrospective study that include patients admitted to the ICU between 1st of April 2013 and 31st of April 2014.

Results. 362 patients were admitted, mean age of 62 years, sex distribution was 1:1 (male:female). Average values for severity score in sepsis at admittance were: SOFA =7, APACHE II=23 and OmegaRO=223.

Medium period of hospitalization was 9.8 days. 29.63% of our patients were mechanically ventilated more than 24 hours. 47.92% of patients received non-invasive ventilation. 28% of patients died.

Of all patients 72.84% were with sepsis/severe sepsis/septic shock/MEOF. Neurologic emergencies (encephalitis/meningitis/stroke) were in 11.63% of cases; 4.15% were cardiologic emergencies (infective endocardites complicated with cardiogenic shock). Acute respiratory failure in patients with chronic obstructive pulmonary disease in 5.54% patients, 6.4% of cases had other pathologies.

Infections with Gram negative germs were diagnosed in 24.32% patients, 14.30% had infections with Gram positive cocci; 15.46% were fungal infection. In 6.62% cases *Clostridium difficile* was the etiologic agent; infection with Gram positive bacillus in 3.6% cases and viral infection in 2.20% patients.

In 5 cases multidrug resistant germs were isolated.

Conclusions. Sepsis is the main cause for patients admittance in our ICU. Because of the complexity of cases a multidisciplinary approach is necessary.

ANTIMICROBIAL PEPTIDES AND BACTERIOPHAGE IN THE TREATMENT OF MICROBIAL INFECTIONS

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Antimicrobial peptides are important components of the innate immune system of every organism. Some of these peptides have proven an antibacterial activity over Gram-positive and negative germs, which has raised interest in an age of increased microbial resistance to current antibiotics. Antimicrobial peptides are small protein molecules composed of only a few amino acids. There are thousands of such peptides, classified according to various criteria. Their action mechanism consists of the disruption of the cellular membrane, followed by the formation of pores and membrane permeability. The main peptides families are: Megainine, Cathelicidine (isolated from neutrophils and epithelial cells), Defensine (Alfadenfensine, Betadenfensine, Gammadenfensine, Deltadenfensine). Prepared drugs: Pexiganan, Plectasin, Brilacidin, Lytxar.

PHAGE-therapy, widely used before the emergence of antibiotics, is making a comeback. The increase of germ resistance to antibiotics has revived this therapy, as an alternative or as a complementarity to the antibiotics therapy. Experimental research on animals have provided promising results in pulmonary infections with *Pseudomonas aeruginosa*. Also the clinical experience - especially that of researchers from Georgia (ELIAVA Institute) - is convincing. PHAGE-therapy is much more targeted (specific) than antibiotics are. It is strictly addressed to the identified pathogen germs, without attacking or destroying the normal flora. In the case of infections with unknown germs, a cocktail can be used, based on presumed etiological criteria. PHAGE-therapy has also been used in skin infections with staphylococcus MRSA, superinfected burns with pseudomonas, chronic skin ulcerations. Drugs which contain bacteriophages have both oral and topic administration (spray). A program has been initiated in Europe entitled PHAGOBURN-multicentric which will start in September 2014 and will target the evaluation of PHAGE-therapy in the case of patients with burns which are candidates for pseudomonas infections.

THE ROLE AND PLACE OF NON-ABSORBABLE ANTIBIOTICS FOR THE TREATMENT OF ACUTE INFECTIOUS DIARRHEA

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The acute diarrheic syndrome is one of the most frequent pathologies in medical practice. Knowing its etiology and pathogenesis is essential for a correct therapeutic approach. We must keep in mind that infectious diarrhea is a physiologic reaction to an aggression represented by an intestinal infection and excessive use of intestinal motility inhibitors must be avoided, and it is even prohibited in the absence of an adequate antibiotic treatment.

In developing countries, acute diarrhea in small children is still a major health problem, responsible for 25% of deaths in children under 5 years old. The "explosion" of tourists travelling to developing countries led to an increasing incidence of the so called "traveler's diarrhea", which affects approximately 40% of the tourists who travel to high risk countries. Non-absorbable antibiotics are currently considered by *the International Society for Travel Medicine* and *FDA* the first choice therapy for prophylaxis and treatment of traveler's diarrhea.

The dramatic increase of antibiotic use in the last years, especially betalactamines and fluoroquinolones, led to a significant increase of post-antibiotherapy diarrhea, including pseudomembranous colitis with *Clostridium difficile*. The use of non-absorbable antibiotics after conclusion of the standard treatment with Vancomycinpo and/or Metronidazolpo has proved to be efficient in preventing relapse.

Treatment principles for diarrheic syndrome include restoring hydroelectrolytic balance, systemic antibiotherapy or non-absorbable antibiotics and diet. After remission of the diarrheic syndrome, the administration of probiotics/simbiotics for the repopulation of the intestinal flora is recommended.

Among non-absorbable antibiotics, rifamixin alpha has an important place because of its wide antibacterial spectrum, low risk of selecting resistant strains and a good tolerability. Comparative studies with system icvs non-absorbable antibiotics proved the lack of inferiority or even the superiority of rifamixin alpha for the treatment of light and mild intestinal infections. Severe forms of disease need to be addressed to a specialist for hospital surveillance and adequate systemic antibiotherapy.

Considering the high incidence of different forms of acute diarrheic disease, the correct therapeutic approach from the debut of the symptoms is essential for reducing morbidity and mortality.

Keywords: acute diarrhea, non-absorbable antibiotics, infectious diarrhea treatment

ANTIBIOTIC PROPHYLAXIS IN SURGERY – REVIEW OF GUIDELINES

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Surgical skin infection (SSI) represents a major cause of mortality and morbidity of the surgical pathology due to prolonged hospitalization and high costs. The most frequent etiology is represented by Gram positive cocci, especially staphylococci but Gram negative bacteria can be implicated also.

The risk of SSI depends on various categories of factors: the risks associated to the surgical intervention like the classification of the surgical wound and the risks associated to the patient's conditions such as the nutrition state like obesity, diabetes, co-existence of another infection, and the immune response of the patient, microbial colonization and history of recent surgical event. Surgical prophylaxis plays an important part in lowering the risk of SSI especially in the presence of various risk factors. The antibiotic prophylaxis has as major parts the timing of the administration, the type of the antibiotic administered, the duration and the costs of the antibiotic prophylaxis.

The implementation of general principles of antibiotic prophylaxis in surgery, taking in consideration all the components, could significantly reduce the risk of SSI, therefore, ideally the antimicrobial agent should be administered in the 30 minute period before the surgical incision, the duration should not exceed 24 hours and for the majority of the surgical interventions one dose regimen is efficient, since multiple doses regimens or post-surgical administration did not proved to be more efficient. The choice of the correct the antimicrobial agent used for prophylaxis must be based on the safety and efficacy profile of the agent, the spectrum, since the broad spectrum antibiotics should be avoided due to the high risk of promoting antibacterial resistance. Cephalosporins are the most commonly used antibiotics in surgical prophylaxis; specifically, cefazolin or cefuroxime are mainly used in the prophylaxis regimens for cardiothoracic surgery, vascular surgery, hip or knee arthroplasty surgery, neurosurgical procedures and gynaecologic and obstetric procedures.

The preferred way of administering the antimicrobial agent is the intravenous way, but topical way is also used: instillation in ophthalmic surgery, pastes or wash-outs.

In conclusion the decision of antibiotic prophylaxis in surgery must be taken considering not only the benefits but also the risks, and the choice of the agent should be according to the guidelines, but individualized for each patient.

Keywords: antibiotic prophylaxis, surgical skin infection, risk factor, antimicrobial agent

HUMAN ORAL MICROBIOME

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The human oral cavity contains a number of different habitats, including the teeth, gingival sulcus, tongue, cheeks, hard and soft palates, and tonsils, harboring one of the most diverse microbiome in the human body. The oral microbiota includes over 600 species (bacteria, viruses, fungi, protozoa, and archaea) with an unequal distribution, different subtypes being prevalent in certain habitats.

Many of these species can associate to form biofilms, which are resistant to mechanical stress or antibiotic treatment. Most are also commensal species, but they can become pathogenic in responses to changes in the environment or other triggers in the oral cavity, including the quality of an individual's personal hygiene.

The complexity of the oral microbiome is being characterized through the newly developed tools of metagenomics such as 16S rRNA cloning which are culture-independent molecular methods. These new molecular methods led to collect 16S rRNA gene sequences into a phylogeny-based database, the Human Oral Microbiome Database (HOMD). The HOMD includes 619 taxa in 13 phyla, as follows: Actinobacteria, Bacteroidetes, Chlamydiae, Chloroflexi, Euryarchaeota, Firmicutes, Fusobacteria, Proteobacteria, Spirochaetes, SR1, Synergistetes, Tenericutes, and TM7. The HOMD is the first description of a human-associated microbiome and provides tools for use in understanding the role of the microbiome in health and oral cavity diseases'.

Individuals' oral microbiomes are highly specific at the species level, although overall the human oral microbiome shows few geographical differences. The bacteria are responsible for the two commonest human bacterial diseases: dental caries and the periodontal diseases.

Although caries and periodontitis are clearly bacterial diseases, they are not infectious diseases in the classical sense because they result from a complex interaction between the commensal microbiota, host susceptibility and environmental factors such as diet and smoking.

Periodontitis, in particular, appears to result from an inappropriate inflammatory reaction to the normal microbiota, exacerbated by the presence of some disease-associated bacterial species. Even though periodontal diseases are initiated by polymicrobial infection, several bacterial species are commonly linked to particular oral diseases.

Besides the two very well-known entities of the oral pathology, the oral microbiome is also associated with systemic diseases, including for instance cardiovascular diseases and atherosclerosis.

The current paper provides an overview of the newest data regarding the taxonomy of oral microbiota, identification methods of the representatives species and their clinical involvement.

SURPRISING DIAGNOSIS IN A PATIENT WITH SECONDARY PULMONARY TUBERCULOSIS

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We present the case of a 32 year old patient, smoker, without history of personal illness, who presented himself in our hospital with cough with purulent expectoration, fever, inappetence, weight loss, asthenia. The symptoms started insidiously 3 weeks before, without improving under the antibiotic treatment, reason for which he was suspected to have an infection with *Mycobacterium tuberculosis*. The patient was directed to our hospital and examination revealed a stable, hemodynamic patient, cachectic, with dry and pale skin, two-sided MV present and fine crackles in the upper right side of the thorax. The laboratory exams revealed severe inflammatory syndrome, mild pancytopenia, mild hepatocytolysis and cholestasis. The BAAR microscopic examination of the sputum was positive, while the non-specific examination detected *Candida* spp. The chest X-rays showed opacity with central hyper-transparency, situated in the right superior lob and hilar adenopathies. We initiated the antituberculosis treatment, standard regimen, with a low response. The abdominal echography detected a hepatosplenomegaly. We stopped temporarily the antituberculosis treatment. Because of the alteration of the clinical state associated with pancytopenia and hepatosplenomegaly, we effectuated the ELISA test to identify the anti-HIV antibodies, which was inconclusive, so we did the Westernblott test, with an intense positive result. The patient was transferred to the Clinical Hospital of Infectious Diseases, where the diagnosis was set: Acute Immune Deficiency Syndrome stage C3 and we began the antiretroviral and antituberculosis treatment, individualised regimen. The patient had a good clinical evolution accompanied by negativation of BAAR examination and CD4 lymphocytes augmentation.

The particularity of this case consists in the atypical clinical evolution of the patient under the antituberculosis treatment, the presence of a single tuberculosis lesion in a BAAR positive patient, the family history of HIV infection and the difficulty of diagnosing the HIV infection.

HIV-RENAL TRANSPLANT YES OR NO?

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HIV has been a major global health problem for longer than three decades now. Since combined antiretroviral therapy (cART) became available, the prognosis of HIV infection has dramatically improved. Previously, HIV-infected individuals died from opportunistic infections. The co-morbidities such as renal insufficiency, coronary artery disease, diabetes mellitus, or liver failure were not significant causes of mortality. Today they are real medical problems for many individuals with well-controlled HIV replication. Liver, kidney, and heart transplantation are treatment options for end stage organ disease. However, HIV infection was considered a contraindication for transplantation because the addition of immunosuppression in an already immunocompromised state, limited supply of donor organs in individuals with unknown outcome. Now the criteria for inclusion on the transplant waiting list are: good compliance on cART, CD4 above 200/cmm and undetectable HIV viremia in the last 3 months, the absence of opportunistic infections in the last 6 months, and the absence of progressive multifocal leukoencephalopathy, chronic intestinal cryptosporidiosis and lymphoma. There are studies made on HIV patients with renal transplant that concluded the transplant is safe and efficient, the viral load remains suppressed, CD4 stable, opportunistic infections are not more often but the acute rejection is more frequent (13-67%).

This case report is about a 44 years woman with diabetes and chronic kidney disease in program of peritoneal dialysis for 8 years, secondary hypertension, and important dyslipidemia. HIV infection was detected in 2006 when she had a pre-transplant investigation. Her HIV viremia was undetectable and CD4: 608/cmm after 6 months of treatment with abacavir, lamivudine and efavirenz, continued for 3 years and abacavir and lamivudine since 2010 until now (nonadherence for efavirenz). Her immunological evolution was very good, with CD4 between 608 and 2414/cmm and viremia <20copies/ml for 7years. The last viremia was 271copies/ml. She did not have opportunistic infections or malignancies. HIV point of view she met the criteria for renal transplant (except the last blip). From an urological point of view the recommended abdominal and pelvis CT scan showed iliac atherosclerosis.

In conclusion in order to improve the quality of life the kidney transplant would be the best option, unfortunately the presence of diabetes and atherosclerosis of blood vessels are important exclusion factors.

A CASE OF PROBABLE FAMILIAL CREUTZFELDT-JAKOB DISEASE

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CJD is a rare spongiform neurodegenerative disease, with an incidence of approximately one case/1 million population per year, invariably fatal, caused by the deposition of prion protein in the brain. It is the most common form of prion disease affecting humans. CJD is reported in almost equal ratios between sexes, although older males (>60 years of age) appear to have a higher incidence of disease. There are 3 general forms: sporadic (85%), familial (5-15%) and acquired (<5%, including variant CJD). It is manifested clinically by rapidly progressive dementia, psychiatric and neurological signs and symptoms (myoclonus, pyramidal, extrapyramidal, visuals and cerebellar signs). We reported a case of 62 year old man who was admitted to our emergency room for: fever (39°C), productive cough, difficulty breathing, swallowing disorders, myoclonus and seizures. Over the past 2 months he gradually developed dysarthria, confusion, difficulty walking, isolation and lack of communications with his family, which were previously diagnosed as vestibule-cerebellar syndrome and cerebral atrophy. Physical examination revealed: malaise, without fever, tachypnea (20 breaths/min), tachycardia (100 beats/min), oxygen saturation 86%, hypotension (110/70 mmHg), right basal lung crackles, aphasia, outlines stiff neck, paravertebral contracture, marked pyramidal spasticity, outlines right Babinski, without swallowing reflex, upper limb myoclonus, generalized seizures. Laboratory investigations revealed: bacterial inflammatory syndrome; normal glucose, electrolytes, liver and renal function; negative Human Immunodeficiency virus (HIV), B and C viral hepatitis, negative syphilis serology (VDRL). The diagnosis of acute meningo-encephalitis was excluded based on lumbar puncture with CSF analysis showing albuminocytological dissociation and negative cultures. CSF 14-3-3 protein assay was positive. Brain MRI revealed hyper signal on DWI and FLAIR sequences in the caudate and lenticular left nucleus, bilateral frontal-basal cortex and left parietal-temporal cortex. Serial EEG recordings demonstrated a specific pattern of 1-2 cycles/sec triphasic slow-wave discharges. In spite of the supportive treatment the patient died as a result of pneumonia and sepsis. The autopsy was not performed. In this case report the diagnosis was supported by characteristic appearance of brain MRI, EEG typical pattern and positive CSF 14-3-3 protein assay in conjunction with the clinical picture according to WHO and CDC diagnostic criteria of CJD. The confirmatory diagnosis requires demonstration of the typical neuropathology or the presents of prion protein in brain tissue obtained at biopsy or autopsy. The patient's granddaughter was in coma with suspicion of CJD indicating a probable familial form of this disorder for which the genetic tests were not performed.

Keywords: familial Creutzfeldt-Jakob disease (CJD), pneumonia, magnetic resonance imaging (MRI), electroencephalogram (EEG), 14-3-3 protein.

CLOSTRIDIUM DIFFICILE COLITIS CAUSING TOXIC MEGACOLON AND SEVERE SEPSIS

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Introduction. *Clostridium difficile* is one of the most common hospital-acquired infections and it accounts for 15% to 20% of all antibiotic associated colitis cases, a significant worldwide nosocomial infection problem. The clinical manifestations of *Clostridium difficile* colitis range from a self-limiting diarrheal disease to fulminant presentations with characteristic pseudomembranes within the large intestine and progression to toxic megacolon, often with fatal complications. This case is remarkable due to patient's comorbidities, difficult therapy choices, multiple recurrences of the severe gastrointestinal symptomatology, negative prognosis and favorable outcome.

Case description. A 47-year-old Caucasian man with a recent medical history significant for *Staphylococcus aureus* sepsis, multiple muscle abscesses (bilateral paraspinal, left psoas), diffuse spinal meningitis of unknown etiology, for which he received prolonged antibiotic therapy, is transferred to our clinic with complaint of fever, acute watery diarrheal syndrome, severe abdominal pain, reduced appetite, fatigue, tachycardia and hypotension. Physical examination was remarkable for abdominal distension and tenderness, urinary and faecal incontinence, paravertebral muscle contractions with lumbosacral pain, absent deep tendon reflexes in left lower limb with diminished sensitivity, no meningeal irritation. Laboratory findings demonstrated inflammatory syndrome, leukocytosis with neutrophilia, anaemia, elevated GPT and gamma-GT, hypo-albuminemia. *Clostridium difficile* toxins were detected in stool sample. He was admitted with a diagnosis of *C. difficile* colitis. Medical management consisted of restriction diet, intravenous rehydration, antibiotic therapy with oral Vancomycin and intravenous Meropenem, corticosteroids. After an initial favorable evolution the initial clinical manifestations reemerge. Abdominal CT scan disclosed coprostasis and inflammation in the colon, ascites. The patient was transferred into surgical service for monitoring and potential colectomy. The patient recuperated after two fecal microbiota transplantations. The clinical evolution was complicated with urinary tract infection symptoms. Urine culture was positive for *Pseudomonas*. Antibiotic therapy with Colistin was initiated and, within five days, it was followed by reemergence of gastrointestinal symptomatology. Colistin treatment was ceased. After ten days of antibiotic therapy with oral Vancomycin and intravenous Metronidazole the clinical evolution was favorable and patient was discharged.

Discussion. This case illustrates the severity of *Clostridium difficile* infection in patients suffering from other comorbid conditions, causing difficulties in choosing therapy for simultaneous different infectious diseases, prolonged hospitalization and potential fatal outcome. Mortality in patients with toxic megacolon, who undergo colectomy with ileostomy, has been reported to be as high as 40%, in contrast with the minimal mortality in medically treated patients. Preventive measures for colonization of hospitalized patients with *C. difficile* must be effectively implemented. Avoidance of unnecessary use of antibiotics is of paramount importance.

STREPTOCOCCUS GALLOLYTICUS ENDOCARDITIS

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Approximately 70% of native valve IE are caused by *Streptococcus spp* including *S. viridans* and *S bovis* (16.7%). *S. bovis* was recently reclassified as *S. gallolyticus*. The gateway for *S. gallolyticus* is the gastrointestinal tract. Bacteremia with or without endocarditis is associated with malignant or premalignant lesions of the colon. *S gallolyticus* endocarditis is different from other endocarditis because it is highly susceptible to intravenous antibiotics and is therefore considered benign; even then it infects valves of patients who are not known to have cardiac valvular abnormalities. We describe the case of a 49-year-old man who was admitted to our hospital with a 4-months history of intermittent high fever, chills and rigors, night sweats, migratory arthralgia and a sudden pain and functional impotence of coxofemoral joint. He admitted to have lost about 10 kg in weight over the same time period. He had no previous history of dental procedures and he did not take any intravenous medications or drugs. He had hypertension but is well-controlled with medications. On examination he was alert, non-toxic, and noted to have mild tegument and cutaneous pallor. His temperature was 36.5°C, pulse rate regular at 80 beats per minute, blood pressure 120/70mmHg, and respiratory rate 18 per minute. There was no peripheral stigmata of infective endocarditis. A faint systolic murmur was heard in the right lower sternal border. The rest of the systemic examination was unremarkable. The laboratory investigation showed a haemoglobin level of 11.1g/dL, white cell count of $6.8 \times 10^3/\mu\text{L}$, platelet count of $143 \times 10^3/\mu\text{L}$. The erythrocyte sedimentation rate was 69 mm/h and C-reactive protein was 11.92 mg/L. All 6 specimens of blood cultures grew *Streptococcus gallolyticus ssp gallolyticus*. The transthoracic echocardiogram revealed multiple florid vegetations attached to the tricuspe aortic valve with moderate aortic regurgitation. The chest radiograph was normal. Computer tomography scan of the abdomen and pelvis reveal moderate hepato-splenomegaly with an area of splenic infarction of 2.3/1.6/1.5 and infarction of left iliac muscles. A definitive diagnosis of *S gallolyticus* endocarditis was made. The patient underwent a colonoscopy which showed a polyp and was excised. The patient improved on antibiotics (ampicillin 12 g/day in combination with gentamicin 160 mg/day, 28 days) and he had surgery after that.

Keywords: endocarditis, *Streptococcus gallolyticus*, complication

THE CASE OF A MAN WITH STILL'S DISEASE

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Introduction: Still's disease is a rare rheumatologic disease, of unknown etiology, but with clinical features resembling infection.

Objectives: Illustration of the case of a man presenting with high fever first seen in the University Hospital of Infectious Disease via the Emergency Department.

Results: A 41 year old man, presented with a possible Still's disease: fever (39° C), "salmon-pink" rash spanning over limbs, torso and face, also with transient arthritis. Laboratory findings showed elevated inflammatory markers, as well as mild leukocytosis with neutrophilia and elevated serum ferritin. Infectious etiologies were excluded and he was transferred to the Clinic of Rheumatology with a presumed adult onset Still's. On admission he exhibited the same symptoms, and after excluding malignant and other rheumatologic etiologies, he received intravenous (IV) Methylprednisolone, followed by oral Prednisone, Methotrexate and Colchicine. After 2 year follow-up the patient is still in remission.

Conclusions: Although Still's disease can present with dramatic symptoms, it has a favourable prognosis, although it may require high-dose corticosteroid therapy. Differential diagnosis with infectious, malignancy and other rheumatologic disease is important prior to safely assuming Still's disease.

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ANAMNESTIC, EPIDEMIOLOGICAL AND DIAGNOSTIC CONSIDERATIONS IN A PATIENT SUFFERING FROM MULTIPLE ORGAN DYSFUNCTION SYNDROME. CASE REPORT.**BIANCA VOINESCU, MIHAELA LUPSE****Clinical Hospital of Infectious Diseases, Cluj Napoca, Romania**

Malaria is a major international public health problem. Although these numbers are decreasing, the numbers of cases of malaria in travelers has been increasing steadily for the past 3 years. Despite the apparent progress in reducing the global prevalence of malaria, many areas remain malaria endemic, and the use of prevention measures by travelers is still inadequate.

We want to present the case of one man, who traveled and worked in the last 2 months in Africa, Guinea, as a constructor. We mention that he had high exposure to mosquito-bites and from his medical history we discovered he took malaria prophylaxis only for a short period of time. Nonspecific onset symptoms (high fever, chills, muscular and articular pain, nausea, abdominal pain), medical history and epidemic control insufficient investigated led to a wrong diagnosis and to a serious, possibly fatal progression of the disease (multiple organ dysfunction syndrome).

Our conclusion is that insufficient malaria prophylaxis lead to the onset of the illness, medical history and epidemic control were of high importance, the delay of an etiological diagnostic led to a late initiation of therapy with serious evolution to multiple organ dysfunction syndrome.

Malaria represents an important public health problem especially in endemic areas, but also in non-endemic area due to the increase in the number of people who travel in tropical countries as well as the low degree of etiological suspicion.

Keywords: malaria, prophylaxis, MSOF

PLANTAR PHLEGMON IN A PATIENT WITH TYPE 2 DIABETES

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Introduction: Infections of the lower limbs in the context of diabetes is a disorder with an increasing frequency and not always leading to a favourable outcome. Diabetes confers a suitable ground for infectious processes by decreasing the sense of touch, proprioception, and decrease of sweating in the legs – specific to sensory phenomena of diabetic neuropathy. The presence of input gates with no pain sensitivity creates opportunities for the emergence of infections of varying degrees of resistance. A complicating factor is the kidney and liver condition of the patient that may limit the therapeutic possibilities of infection.

Case presentation: Patient aged 62 years, onset of type 2 diabetes about 11 years before, treated with insulin since 2006, currently in basal and symptomatic hyperuricaemia without signs and symptoms of chronic arterial legs is hospitalized in Diabetes and Metabolic Diseases Centre Cluj Napoca for the emergence of a right leg ulcers, toes I, II and dorsal and plantar foot phlegmons respectively, occurred last week. The risk factors for ulceration present: sensory diabetic neuropathy with total lack of sense of touch and vibration, dyslipidaemia, hypertension, chronic moderate alcohol consumption, overweight – therapeutic neglect. On admission: general influenced telangiectasia in the cheeks, taters gouty joints present in the small and large balanced cardio-respiratory, BP = 113/71 mmHg, AV = 81/minute, abdomen free. Local: unilateral knee swelling, signs Celsiene present. Biological: leucocytosis at the upper limit of normal, moderately elevated inflammatory evidence. Harvest wound secretion and begin treatment based on antibiogram Hospital of Alba Iulia, where he was admitted earlier, Cefamyl 2g/day for Klebsiella. After three days of steady progress surgical cure wound phalanx and metatarsal amputation of toes I, II and III, the result from wound secretion evidenced positive for Morganella Morgagni. The patient presented with fever, with relatively good general condition, without signs of sepsis. Biological: mild leucocytosis, CRP = 15.6, fibrinogen = 865, mixed dyslipidaemia, impaired renal function, moderate anaemia. Decision is for the antibiotic and low kidney function continued therapy with Piperacillin Tazobactam, continuing the initial parenteral therapy. Further development at home is slightly favourable in the beginning. After a few weeks Staphylococcus aureus infection is observed. Henceforth the patient is monitored for progress.

Conclusion: It is difficult to treat infection with a germ resistant to most agents in the case of a patient having decreased renal function with relatively short development time. High risk of superinfection is plagued with poor healing tendency.

STILL'S DISEASE - AN ATYPICAL CASE PRESENTATION

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Introduction: Still's is a rare rheumatologic disease characterized by fever, joint pains and a typical rash, often mimicking an infection in clinical appearance, making Infectious Disease Clinics frequent first stops for these patients. In this case, a woman was admitted to the University Clinical Hospital of Infectious Diseases for fever and severe joint pains. This case is remarkable because the patient's admission during winter made respiratory infection a likely diagnosis, even more so because she lacked the typical rash exhibited in up to 94% of Still's cases.

Case presentation: a 39-year-old woman was admitted in February 2014 (flu season) presenting fever (39.5o C) with severe upper body joint and muscle pains, headache and mild cough. Laboratory findings included elevated inflammatory syndrome, neutrophilia with modest leukocytosis and slightly elevated liver enzymes. She received broad-spectrum antibiotics, as well as Oseltamivir, with no favourable response. Although infectious etiologies were gradually excluded and antibiotherapy spectrum was extended, symptoms persisted until Dexamethasone was added to the treatment plan, at which point the fever dropped and the joint pains diminished considerably.

At that point adult onset Still's disease was taken into consideration and the patient was transferred to the Clinic of Rheumatology. On admission there, symptomatology was mildly improved, ferritin levels were slightly elevated and routine blood tests corroborated findings from the Infectious Disease Hospital. After excluding malignant haemopathies and other rheumatologic diseases, she received IV Methylprednisolone, followed by oral Prednisone, Methotrexate and Colchicine. She responded favourably, in remission after 6 month follow up.

Discussion: this case illustrates some of that challenges encountered in diagnosing Still's disease in a paucisymptomatic patient admitted during flu season. Exhaustive serologic testings were needed to exclude infectious etiologies before Still's could be considered and corticosteroid therapy safely started.

INFECTIVE ENDOCARDITIS - ETIOLOGICAL DIAGNOSIS CHALLENGE

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Subacute endocarditis is difficult to diagnose due to lack of major Duke diagnostic criteria, in some cases. This is a case presentation of a 63 years old male, known with aortic regurgitation and hypertension, that was hospitalized in our department for fever accompanied by chills and night sweats, for which he followed various antibiotic treatments, with the resolution of symptoms during the treatment, but recurrence of fever in about 3 days after treatment ended. At admission in our service- patient in relative good health, febrile, pale, multiple dental foci, systolic heart murmur and no other significant changes. 3 pairs of blood cultures were harvested, before antibiotic treatment was started, which came back positive for *Francisella tularensis*, repeatedly performed echocardiography showed degenerative modifications of the aortic valve. Clinical, epidemiologic data and laboratory investigations argue for subacute infective endocarditis, but blood cultures argue for typhoidal tularemia. Antibiotic treatment was started with Vancomycin- 28 days, and for the possible tularemia Gentamicin- 14 days is associated. After 21 days of treatment control blood cultures were harvested, which showed the same Gram negative bacterium, identified with VITEK (99% specificity), the decision was taken to use another identification method, MALDITOF, which identified it as *Aggregatibacter acetinomycetemcomitans*, a Gram negative coccobacillus, a member of HACEK group endocarditis, present in the peridontal plaque. The final diagnosis was HACEK group subacute infective endocarditis and antibiotic treatment with Ampicillin 12g/day- 28 days was administered with the resolution of symptoms and no more recurrence. This case presentation highlights the etiological diagnosis challenges in HACEK group endocarditis.

CLOSTRIDIUM DIFFICILE COLITIS RESISTANT TO STANDARD THERAPY

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Background & Aims: Frequent use of antibiotics has increased the incidence of *Clostridium difficile* (CD) colitis. The cost of this disease is high. Recurrence occurs in 25% of cases after correct treatment (1). The study objective was to investigate the efficacy and the safety of faecal transplant (FT) in patients with CD infection resistant to drug therapy.

Patients and methods: Five patients, diagnosed with CD colitis resistant to standard therapy with Metronidazole and Vancomycin, were included in the study. In all cases, 250 ml solution (faeces diluted 1:5 to saline solution) was infused into the terminal ileum.

Results: Diarrhea was reduced by 75% in all patients in the next five days after administration. One patient had a recurrence, 5 weeks after FT. The treatment was well tolerated in all cases. One patient had mild fever, 24 hours after treatment.

Discussion: FT has a high cure rate in case of patients diagnosed with CD colitis. Recurrences and side effects after FT are uncommon.

Conclusions: FT may be an effective and safe alternative treatment for colitis with CD resistant to standard treatment.

Acknowledgement: Authors have no conflicts of interest.

Keywords: *Clostridium difficile*, colitis, faecal transplant.

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THE PROFILE OF CLOSTRIDIUM DIFFICILE INFECTED PATIENT

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Introduction: *Clostridium difficile* infection (CDI) is a major health problem through its presence in both community and hospital conditions, the risk of complications, recurrence, resistance to treatment leading to increased costs and mortality.

Objectives: To analyze demographic, epidemiological, clinical data and evolution of patients (Px) admitted with ICD.

Methods: Observational, retrospective (January-June 2014) study, on 56 Px admitted to the Infectious Diseases Clinics of Hospital Victor Babes Craiova diagnosed with ICD.

Results: General study group: median age, 66 (IQR 16-87) years, with a balanced gender distribution (M: F = 1: 1), the median duration of hospitalization - 7 (IQR 2-16) days. Comorbidities were identified in 75% Px with ICD. Epidemiological history showed that 44.64% were nosocomial cases, ICD indefinite - 32.14% and community ICD - 23.21%. The diagnosis was: ICD certain - 16.07% of the cases, in 83.93% ICD was likely. Sepsis was identified in 33.93% of Px. ATLAS score could be assessed for 48 Px, with a median of 2 (IQR 0-7). ICD - recurrence was identified in 7.14% of the study group. Unfavorable development was recorded in 12.5% of cases (1.79% of Px dying, the rest being transferred to the intensive care unit).

Conclusions: ICD most commonly affects older Px, associating comorbidities. ICD is often of nosocomial origin. The clinical form of presentation of the ICD may be severe, a significant proportion of Px meeting the criteria for sepsis. The evolution of ICD is encumbered by the risk of relapse and may be life threatening.

Keywords: ICD, nosocomial, sepsis, relapse.

DIGESTIVE CANDIDA PREVALENCE IN THE CLOSTRIDIUM DIFFICILE INFECTION (ICD)

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Background & Aims: Clostridium difficile (ICD) is the most common cause of nosocomial infection and is associated with increased morbidity and mortality. The study sought to evaluate the incidence of Candida infection associated with ICD in our service and risk factors associated with relapses.

Patients and methods: This is a retrospective analysis of cases of Clostridium difficile infection in patients admitted to the Infectious Diseases Section Oradea during the period 01.01.2012-31.03.2014. We excluded all cases where data were not sufficient to support the diagnosis of ICD. We noted demographics, clinical risk factors (antibiotics, chemotherapy, corticosteroids, in combination with proton pump inhibitors, PPIs).

Results: At the time mentioned above, there were 107 cases of patients with ICD diagnosis supporting on determining Clostridium difficile toxin A & B positive. About one third of them (31.78%) were observed with concomitant infection by Candida by bacterial examination performed on admission to the hospital. Of all cases with ICD, 55.14% were women, most of them from Oradea. Most cases were elderly patients, 74 (69.15%) were over 56 years old, and 73.83% had a recent history of surgery or hospital treatment. Over 16.83% followed antibiotic treatment and/or IPP at home. There were various forms of disease, ranging from mild gastroenteritis colitis, pseudomembranous colitis and toxic megacolon, some with fatal outcome (2 cases). Therapy included rifaximin and metronidazole (oral) for mild cases (21 cases), glycopeptides (oral) ± metronidazole oral/intravenous moderate to severe cases. There were 26 cases of developments with relapses (24.29%).

Conclusions: The incidence of CDI has increased dramatically in our service in the last quarter of 2013 and first half of 2014, compared to 2012/2013. ICD occurrence in the elderly, especially with co-morbidities and after treatment with antibiotics, especially followed in the hospital are the main factors leading to the emergence of Candida infections in hospitalized patients in the ward, and the treatment is usually associated ICD therapy and anti-candida.

PYLEPHLEBITIS WITH PYLETHROMBOSIS, RARE CAUSE OF FEBRILE SYNDROME. CASE REPORT

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Background & Aims. We present a particular case of prolonged febrile syndrome of rare etiology.

Patients and methods. A 44 years old patient, an officer from urban area, was admitted to the Infectious Diseases Clinic in Oradea because of a 7 days lasting febrile syndrome. In order to establish the diagnosis, clinical, laboratory and imaging investigations were performed.

Results. The patient was hospitalized in the Infectious Diseases Clinic in Oradea, after a week of outpatient treatment with Levofloxacin 500 mg day for repeated feverish chills. On admission, the patient shows scleral jaundice, fever, chills, abdominal pain in the right hypochondrium, myalgia. Laboratory results: ALAT: 62 u/l, ASAT: 52 u/l, GGT 650 U/l, negative blood culture and serology for leptospire. Abdominal ultrasound reveals only a malformed gallbladder. After 4 days of treatment with Cefoperazone / Sulbactam 2x2g/day + Ciprofloxacin 2x200 mg/day (IV), the general condition of the patient remains stationary. Repeated abdominal ultrasounds reveal inflammation of the portal vein (pylephlebitis) with a thrombus shape about 2 cm from the superior mesenteric vein (pylethrombosis) and a diverticulum in the descending colon. Following the administration of Meropenem 3x1g/day + Gentamicin 2x80mg/day + Metronidazole 3x500mg/day + Nadroparin 2x 0.4 ml/day for 10 days, continuous improvement of clinical symptoms and biological samples is recorded.

Conclusions. We emphasize the importance of the imaging criteria for the most accurate diagnosis of a prolonged febrile syndrome occurring in a male patient, as well as the use of broad-spectrum antibiotics and the use of the combination of antibiotics, respectively.

Keywords: pylephlebitis, pylethrombosis, superior mesenteric vein, antibiotics

THE ROLE OF MEDICAL REHABILITATION IN THE CAUDA EQUINA SYNDROME WITH FLACCID PARAPARESIS AFTER SPINAL MENINGITIS. A CASE REPORT

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Patient L.I., aged 47 years, with multiple hospitalizations in November 2013 for multiple neurological and infectious diseases. In October 2011, surgery had been performed for vicious posttraumatic right acetabular callus, confirmed by computed tomography. Subsequently, in November 2013, the patient had lumbar pain radiating to the lower limbs, functional impotence, sphincter incontinence, septic state with positive hemocultures for *Staphylococcus aureus*, with multiple paravertebral abscesses involving the left iliopsoas muscle, confirmed by contrast magnetic resonance imaging of the dorsolumbar spine, operated phlegmon of the left leg, which were interpreted as diffuse secondary spinal meningitis, complicated by a cauda equina syndrome, for which adequate antibiotic treatment was administered at the Clinic of Infectious Diseases Cluj-Napoca. The patient also presented two episodes of *Clostridium difficile* acute enterocolitis, with two fecal transplant sessions. In May 2014, the patient was admitted to the Rehabilitation Hospital Cluj-Napoca for motor deficit of the lower limbs, walking disorders, micturition disorders, sexual dynamic disorders, pain in the lumbar spine radiating to the lower limbs, sudden onset sensitivity disorders at D10 level in a febrile context in November 2013, interpreted based on lumbar MRI as spinal meningitis secondary to dorsal and lumbar paravertebral abscesses. During the course of hospitalization, the patient received a complex medical rehabilitation treatment consisting of kinetotherapy (posturations, passive mobilizations, active mobilizations, transfers, proprioceptive neuromuscular facilitation techniques, walking rehabilitation, respiratory gymnastics, rehabilitation of sensitivity disorders), occupational therapy, massage, medium frequency currents for the rehabilitation of micturition disorders, with good results particularly in walking and urinary incontinence rehabilitation. The aim of the presentation of this case is to emphasize the fact that rehabilitation programs using physical-kinetic therapeutic methods are the only way to limit functional deficit, playing an important role in the long-term management and care of the patient. The particularity of this case consists of the fact that the patient is young, without a known personal pathological history, and symptoms occurred two years after orthopedic surgery, with sudden motor deficit in the lower limbs. The regular follow-up of the patient and his inclusion in complex medical rehabilitation programs in order to limit the functional deficit, increase the autonomy and improve the quality of life of this patient are important.

Keywords: paraparesis, rehabilitation, spinal meningitis

PROTECTIVE AND RISK FACTORS RELATED TO THE THERAPEUTIC ADHERENCE TO ANTIRETROVIRAL REGIMENS

GEORGE-MIHAI CĂLIN, CORINA ITU

Background and aim. The introduction of combined therapy has offered people living with HIV the chance to have a long lifespan, but this goal could be achieved only if patients adhere to medical regimens. Medication adherence is considered a health related behaviour which may be influenced by factors as the quality of therapeutic relationship or patients history of infection with HIV. This study aimed to identify the connection between psycho-social factors and therapeutic adherence to antiretroviral medications.

Patients and method. The sample consisted of 89 patients receiving antiretroviral medications. The design of the study was cross-sectional. The data were collected using a questionnaire that included questions on socio-demographic characteristics and aspects about patients experience related to HIV. The variables of the study were quality of social support, quality of the therapeutic relationship, self-efficacy level, and illness perception. Adherence was assessed using the revised Adult AIDS Clinical Trials Group Scale, a lower score indicating adequate adherence to treatment.

Results. The level of adherence in the sample was satisfactory with an average score of 7.30 points. Patients stated as main reasons of low adherence unexpected changes of daily routine, fear of being exposed, forgetting about taking medication, feelings of sadness. It was found that there was a significant relationship between adherence and the quality of the relationship with the infectious diseases doctor ($p=0.024$); patients with a high level of personal self-efficacy recorded optimal adherence ($p = 0.002$). The study highlighted a positive correlation between adherence to medical regimen and illness perception ($p = 0.048$). ANOVA analysis revealed significant differences in adherence level depending on the length of treatment and the period of diagnosis.

Discussion. The data showed that the factors which might support therapeutic adherence were related to the quality of social support, patients receiving family support recorded optimal levels of adherence. Another factor that was identified as protective was the quality of the therapeutic relationship, patients who perceived themselves engaged in the therapeutic relationship displayed optimal adherence. The study evidenced the fact that illness perception impeded medical adherence, patients who perceived HIV infection as threatening, recorded poor adherence level.

Conclusion. The study indicated that therapeutic adherence is linked to the patients' way to relate to HIV infection, those who perceived themselves as competent to manage their condition recorded satisfactory adherence. The data also revealed that patients at risk of poor adherence were patients with a long history of infection, such as multiple medication regimen and a long period of taking antiretroviral medications.

10 YEARS OF PSYCHOSOCIAL ASSISTANCE FOR HIV POSITIVE INDIVIDUALS

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Over 30 years ago the medical community found itself facing a new challenge: the human immunosuppressive virus. Although initially approached solely from a medical perspective, subsequent events have highlighted the fact that HIV/AIDS infection is more than a "chronic infection" and that it triggers devastating psychological, social and economical consequences. People facing this challenge often go through dramatic episodes, hence the necessity to expand the medical team with specialists from various activity fields such as social workers and psychologists.

The purpose of our study is to provide an overview of the social and psychological services that The HIV Regional Evaluation and Monitoring Centre Cluj offers its patients.

Social work and psychological services for HIV positive patients have been offered within The Infectious Diseases Hospital since 2004. These services have been developed and implemented by Romanian Angel Appeal Foundation through a project financed by The Global Fund to Fight AIDS, Tuberculosis and Malaria. The project has been developed between July 2004 and March 2006 as a partnership among The Infectious Diseases Hospital, Cluj-Napoca and The Centre for Public Health Cluj. Starting March 2006 the psycho-social personnel has been integrated within the HIV/AIDS Clinical Compartment of The Infectious Diseases Hospital.

The existence of multidisciplinary assistance services such as medical, social and psychological, allow a complex and efficient monitoring of the HIV positive patient resulting in increased adherence to retroviral treatment and life quality improvement. Through the measures that they have taken the psycho-social professionals have contributed to the educational, social and professional reintegration of HIV positive patients, as well as reduced number of discriminative situations and social exclusion.

ETIOLOGICAL DIAGNOSIS OF ACUTE DIARRHOEA IN CHILDREN. THERAPEUTIC CONSIDERATIONS

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Background. The causes of infectious acute diarrhoea (IAD) include a wide etiological spectrum. Most cases are self-limiting and require the prevention and control of dehydration. Antibiotic treatment is indicated in few cases, otherwise in most cases is useless or can increase complications risk.

Aim. Evaluation of IDA etiology and therapeutic implications for hospitalised patients during an 11-month period (July 2013 – June 2014).

Material and methods. There were performed 2014 stool cultures and 1221 Rotavirus /Adenovirus antigen assays (immunochromatographic tests). We used the following culture mediums: hektoen enteric agar plates and Selenite broth (for Salmonella, Shigella), MacConkey agar for Enteropathogen E.Coli (EPEC) and Entero-hemorrhagic E.Coli (EHEC), CIN (for Yersinia), CCDA (for Campylobacter). Other tests used: latex-agglutination (screening Salmonella), multi-test medium (MIU, TSI), "O" antisera agglutination (for Salmonella, Shigella, Yersinia, EPEC, EHEC confirmation), Gram stain stool exam (for Campylobacter confirmation) and Vitek cards. Positive control stool cultures were excluded.

Results. The authors obtained 211 positive results for Rotavirus, 50 for Adenovirus, 82 positive stool cultures for Campylobacter, 66 for Salmonella, 11 for Shigella, 5 for EPEC and no positive result for EHEC.

Conclusions. 1. Viral etiology was the most frequent, in accordance with literature data; in these cases the antibiotic treatment is not recommended; 2. Campylobacter spp represented the most frequent bacterial etiology. The antibiotherapy reduces not only duration of symptoms but also the environment spreading risk. The antimicrobial sensitivity test is not easy to perform and macrolides are the first choice therapy; 3. In uncomplicated Salmonella gastroenteritis (second bacterial etiology) antimicrobial therapy is not recommended; 4. The authors noticed quite frequent positive results for Shigella and Yersinia and all isolates should be tested for antimicrobial susceptibility; 5. There were diagnosed 5 EPEC cases and no EHEC case. The authors recommend using Shiga-toxins detecting methods for Shiga-toxins E.Coli because its incidence is increasing and antibiotherapy is contraindicated.

Keywords: infectious acute diarrhea, child, etiology, treatment.

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PRACTICES IN THE INFECTIOUS DISEASES HOSPITAL FOR THE ADULT POST-STREPTOCOCCAL SYNDROMES

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Background & Aims. The streptococcal infections frequently occur during childhood, their sequelae called post-streptococcal syndromes being diagnosed at teen ages and adulthood; they represent a borderline pathology between many internal medicine specialties (including the infectious diseases). As the main objective is to diagnose and treat those entities, a correct clinical and test interpretation and antibiotic prescription are necessary.

Patients and Methods. I retrospectively studied the post-streptococcal syndromes admitted into the Army's Infectious Diseases Ward within the last 10 years. Most of the patients were twice yearly monitored clinically and biologically, by inter-disciplinary approaches, sometimes medical and surgical (e.g. for endocarditis).

Results. I identified and treated minor post-streptococcal (e.g. raised ASO, recurrent rashes) as well as major (e.g. endocarditis) conditions. I described the forms of the streptococcal infections (self-limiting) as well as the post-streptococcal syndromes (monophasic, and multi-recurrential) and I established a unitary therapeutical conduct for the treatment and the secondary antibiotic prophylaxis

Discussion. The antibiotic treatment is essential to eradicate the remnant infectious focuses: as using two doses of Benzathin Penicillin G (MoldaminR) every 5 days, every 10-14 days for the secondary prophylaxis. The length of the secondary prophylaxis, for months-years, remains a debated problem, but the clinical improvement, the reduction of the inflammatory phenomena, the ASO dropping tendency is helpful.

Conclusions. Classifying the clinical and evolutive forms of the streptococcal infection is useful for the therapeutical approach.

Acknowledgements: To my mother, a retired Consultant Pediatrician

Keywords: streptococcal infections, antistreptolysin O (ASO), prophylaxis

NERVOUS SISTEM TUBERCULOSIS – A CLINICAL CASE

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Tuberculosis in the brain can take a variety of forms and raises problems of differential diagnosis.

Clinical case: Patient sex M, aged 44 years, with type 1 diabetes is diagnosed in Italy with suspected pulmonary TB and TB chest X-ray and cerebral CT. After performing brain and thorax remains the suspicion of TB and start specific treatment. Therapy of ischemic stroke occurring disorders with impaired general condition and hemiparesis. Is evaluated in the Neurology Service, which adds to the specific therapy, treatment, antifungal, antiparasitic plus Moxifloxacin, and is transferred to the Intensive Care Service. After a few days the evolution is favorable, the patient becomes cooperative and transferred to a ward in the Infectious Diseases Unit.

On admission, the patient was easily confused, drowsy PL-CSF discrete changes (25 elements and biochemistry modified). The repeated brain CT, with the description of vasculitic lesions.

We discuss the issue of differential diagnosis and the evolution under treatment.

THE ABSCESS - A RARE PITUITARY PATHOLOGY

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Background. With 250 cases described in literature, pituitary abscess is a rare pathology, having major morbid potential. The atypical clinical presentation characterized by the paucity of infectious features makes it difficult to have a preoperative etiological diagnosis. On the other hand, the lethal risk requires a correct diagnosis and treatment.

Case report. We report a case of a 15-year-old girl, who presented with a 6 months headaches history, central thyrogonadic insufficiency and diabetes insipidus, without infectious features or visual impairment. The MRI examination revealed a 2 cm cystic pituitary mass with ring enhancement. Trans-sphenoidal neurosurgical drainage established the diagnosis of primary pituitary abscess and the bacterial cultures revealed infection with *Streptococcus* spp. Postoperatively, the patient underwent antibiotic treatment for 4 weeks, initially i.v. and then oral, and substitution therapy with desmopressin. One year after surgery, recovery of diabetes insipidus and of the pituitary insufficiency was documented, with the persistence of subnormal growth hormone secretion, and magnetic resonance imaging revealed an empty sella.

Discussion. After reviewing the literature, we present the clinical and imaging features that increase preoperative diagnostic accuracy.

Conclusions. The etiological treatment is essential and it consists of transsphenoidal surgical evacuation followed by long-term antibiotic therapy. The anterior pituitary insufficiency and the diabetes insipidus usually cure or improve.

Keywords: abscess, pituitary gland, *hypopituitarism*, diabetes insipidus

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CURRENT ETIOLOGICAL TREATMENT OPTIONS IN ESCHERICHIA COLI URINARY TRACT INFECTIONS IN BRASOV COUNTY

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Background and aims: Urinary tract infections are common in the medical practice of different medical specialties, caused in most of the cases by *Escherichia coli*. The currently treatment is empirical, based on etiological likelihood and antibiotics susceptibility. An important and present medical problem, over the world and in Romania too, refers to resistance rates of *Escherichia coli* strains to antibiotics, that can differ from region to region and can determine the success or failure of treatment. Thus the choice of antibiotic should be based on knowledge of current local resistance profiles of *E. coli* strains to antibiotics. The aim of this study was to evaluate the current antibiotic susceptibility of *Escherichia coli* strains isolated from urine cultures in Brasov county.

Materials and methods: Retrospective study, which analyzed 62 community strains of *Escherichia coli* from significant urine cultures of patients admitted to the Infectious Diseases Hospital in Brasov with urinary tract infections during the period September 2013 to June 2014. Antibiotic susceptibility testing was performed by disc diffusion method for the following antibacterial: ciprofloxacin, ceftriaxone, ceftazidim, cefuroxime, amoxicillin/clavulanic acid, trimethoprim/sulphamethoxazole, gentamicin, colistin, meropenem.

Results: The susceptibility of the tested strains was 72.58% for ciprofloxacin, 87.27% for ceftriaxone, 98.39% for ceftazidime, 86.27% for cefuroxime, 68.42% for amoxicillin + clavulanic acid, 62.96% for trimethoprim, 81.497% for gentamicin, 92.31% for Colistin and 100% for meropenem. Resistance to 2 antibiotics have met at 16.13% of cases, to 3 antibiotics to 6.45% of tested strains and to 4 and more than 4 antibacterial at 4.84% of the cases.

Conclusions: 1. For the *Escherichia coli* strains circulating in Brasov we found lower rates of susceptibility to antibacterial commonly used in outpatients medical practice (ciprofloxacin, trimethoprim-sulfamethoxazole, amoxicillin + clavulanic acid), a situation that may lead to treatment failure. 2. Susceptibility of *Escherichia coli* strains remains high to second-generation cephalosporins (cefuroxime) and especially to the third generation, to Gentamicin, colistin and meropenem. 3. Periodic studies are required to assess the susceptibility of the local circulating strains of *Escherichia coli*, for choosing the correct therapeutic decision to allow healing and avoid installation of bacterial resistance to antibiotics.

Keywords: urinary tract infections, *Escherichia coli*, antimicrobial susceptibility

CLINICAL AND BIOLOGICAL ASPECTS OF PATIENTS DIAGNOSED WITH LYME DISEASE IN BIHOR COUNTY BETWEEN 2012-2013

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Background & Aims. The aim of this study was to examine the dynamic evolution of the clinical and biological manifestations of Lyme disease.

Patients and methods. The study group comprised 160 patients who presented at the Infectious Diseases Clinic in Oradea between 2012 and 2013 for a tick bite. ELISA was used for the detection of Lyme disease followed by confirmation by means of Western-blot method.

Results. A quarter (25.6%) of patients with tick bites were diagnosed with Lyme disease, mostly from urban areas (73%). All patients with Lyme disease were in the 1st stage of the disease. A significant proportion of patients were diagnosed in the summer months, from July to August (82%), perilesional erythema (90%) being the most common sign, sometimes accompanied by myalgia and arthralgia. The disappearance of perilesional erythema was the most frequently reported sign after 2-3 weeks of starting antibiotic – Doxycycline for adults and Amoxicillin for children. Borrelia IgM antibodies negative results were more frequently noted after 5-6 months from presentation (65%).

Conclusions. Lyme disease is a disease with high incidence among patients with tick bites, a quarter of them presenting suggestive clinical-biological manifestations of Lyme disease.

Keywords: ELISA, Western Blot, Borrelia, Lyme

THE LISTERIA MONOCYTOGENES INFECTION - CLINICAL FEATURES AND EVOLUTION IN NON-HIV IMMUNOCOMPROMISED PATIENTS. CASE PRESENTATION

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Introduction. *Listeria monocytogenes* is the third cause of bacterial meningitis in adults over 60 years, and it is also common in immunosuppressed patients.

Objective. Specifying the clinical features and the evolutionary process of *Listeria monocytogenes* infection with non-HIV immunocompromised patients.

Case presentation. 59 years old female with known B cell chronic lymphocytic leukemia stage CIII, postmedicamentous autoimmune hemolytic anemia (Fludarabine), hypothyroidism, with ischemic heart disease and hypertensive, diagnosed with infection with *Listeria monocytogenes*. The patient was admitted for fever, stiff neck, headache, convergent strabismus on the left eye, confusion, ataxia, diminished global tendon reflexes and Babinski on left side. MRI brain pleaded for ischemic stroke in the left anterior cerebral artery territory. The lumbar puncture showed cerebrospinal fluid with pleocytosis of 829 leukocytes, CSF glucose of 10.2 mg/dl, CSF protein level of 111.2 mg/dl, positive cultures for *Listeria monocytogenes*. The blood culture was also positive for *Listeria monocytogenes*. The evolution of sepsis and acute meningoencephalitis with *Listeria monocytogenes* under antibiotic treatment with ceftriaxone, ampicillin, and ciprofloxacin was favorable and the patient was discharged on the 21st day of hospitalization.

Conclusions. Combination therapy with fludarabine and prednisone in patients with chronic lymphocytic leukemia increases the risks of listeriosis. Adding a neurological picture to the meningeal syndrome is more common in meningoencephalitis caused by *L. Monocytogenes*, than in the bacterial meningoencephalitis caused by other etiologies. *Listeria monocytogenes* generates invasive infections in immunocompromised patients.

Keywords: *Listeria monocytogenes*, immunocompromised patients

CEREBRAL ABSCESES IN IMMUNOCOMPETENT PATIENTS

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Aims. Outlining the ethiopathogenic, clinical and therapeutic characteristics of cerebral abscesses in immunocompetent patients.

Patients and Methods. This is a retrospective study including cases of cerebral abscesses diagnosed between January 2009 and December 2013 in the Infectious Disease Clinical Department, Targu Mures.

Results. Eleven cases of cerebral abscess were included in the study. The gender distribution was uneven (7 males and 4 females); 6 patients were living in rural and 5 patients in urban areas. The most affected age groups were 25-45 (4 cases, 36.36%) and 7-15 (3 cases, 27.27%). Solitary cerebral abscesses were predominant (9 cases); 2 patients had multiple abscesses. Most frequently the frontal and temporal lobes were involved (3 cases each) followed by the brain stem (2 cases), cerebellum parietal and frontal lobes (1 case each). Two abscesses were recurrent (2 and 3 episodes) leading to multiple surgical interventions. The most frequent way of propagation was by contiguity from neighbouring infectious processes (etmoidal or fronto-etmoidal sinusitis – 2 cases, chronic purulent otomastoiditis – 3 cases and 1 nasal abscess); in 4 cases the abscesses were idiopathic and in one case secondary to bacterial meningitis. The abscesses secondary to etmoidal foci were frontal and those secondary to otomastoiditis were temporal or cerebellar. The etiology as established by bacteriological examination of the intraoperative fluid specimens included *Propionobacterium*, *Streptococcus salivarius*, *Streptococcus betahemolyticus* group C, *Enterococcus fecalis*, mixed anaerobic flora, in two cases identical with the one identified in the cholesteatoma. The clinical picture was mainly infectious syndrome, intracranial hypertension syndrome, paralysis/paresis, cerebellar syndrome, paresis of the cranial nerves III, IV and VII, aphasia, dizziness, coma. The mean interval from onset of symptoms to hospital admission was 10 days (2 to 20 days). Seven patients (63.63%) required surgery with favorable outcome; the most used antibiotics were Vancomycin and Ceftriaxon (72.72%), Meropenem (63.63%) and Ciprofloxacin (54.54%). Admission to the Infectious Diseases Unit preceded surgery (5 patients), followed it (2 patients) or both (2 patients).

Conclusions. Cerebral abscesses affected mainly young adults and adolescents and were usually due to propagation from unattended neighboring infectious foci. Their localization was influenced by the primary infectious site. The onset of symptoms was often mild therefore the diagnosis was often late. Efficient therapy of cerebral abscesses requires close interdisciplinary cooperation.

Keywords: cerebral, abscesses, immunocompetent

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