NATIONAL CONFERENCE OF INFECTIOUS DISEASESES

CRAIOVA, 7-9 MAY 2015

The threat of microbial resistance to antibiotics - peculiarities and regional solutions
Antiviral therapy in Romania - accessibility, performance and limits
Vary

ABSTRACTS

DOI: 10.12865/CHSJ.42.03.12

MECHANISMS OF BACTERIAL RESISTANCE TO ANTIBIOTICS

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English abstract not available

GUT MICROBIOME AND THE RESISTANCE TO ANTIBIOTICS

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Human gut contains the most complex and vast microbial ecosystem known so far (intestinal/gut microbiome, IM). It has been compared to an "microbial organ" with an impressive range of quantitative and functional features: weight approx. 1.1 -1.5 kg, high cellularity (approx.100 trillion microbes or 10^{11}--10^{12} germs/g gastro-intestinal content), microbial unique species > 1000; a whole genome enormous - 3.3 million non-redundant genes).

As regards IM functions, they are related to the microbial metabolism and final degradation products. Far from being of marginal importance, functions (i.e. metabolic, protective, immune, structural) are extremely complex, and some are indispensable for the human host.

Composition, abundancy, diversity and architecture of IM is disturbed by many factors endogenous or externally, among them antibiotics having a very important position.

Resistance to antibiotics (RAB) is coded genetically, and can be *intrinsic* (expressed as virtual of all strains of bacterial species) and *acquired* (limited to sub-populations of a certain bacterial species).

The content of genes for resistance to antibiotics (GRAB) at IM level is impressive (a true " internally resistome "), in conjunction with an enormous potential for the transmission of resistance to the offsprings or to permanent or transient partners of habitat.

The phenomenon RAB is not new, it has developed along the evolution of germs, a long time before synthesis by man of antibiotics, as a mechanism for survival at the ecological level in face of aggression of antimicrobial substances produced and disposed in the environment by other germs.

There were found at nutural sites older than 4 million years bacteria with multidrug resistance genes (Bhullar K, 2012) or in the permafrost sediment, older than 30 000 years, in northern British Columbia (Products(Modi, S. R, 2014). These data suggest that antibiotics were scattered throughout natural external environment and genes of resistance to they are moving for thousands of years ago.

So it is not surprising that in IM there is germs with *intrinsic resistance* to one or more antibiotics. In man, colonization with resistant intestinal bacteria appears in the first 3 days after birth (Koenig, JE, 2011). Phenotypes of resistance have been proved in separate populations with limited exposure to antibiotics (Bartoloni, A. 2004).

In colonic melting-pot, maintenance of RAB within microbial consortia is a complex and permanently phenomenon. Development of RAB may be made by *mutations* of bacterial gene content and, in particular, by *horizontal gene transfer* (HGT) between bacteria, of the same species, but also species more or less related. Genetic material of resistance represents 15-20 % of prokaryotic genomes (Koonin EV, 2001).

In HGT, the resistance propagates through *conjugation*, *phages transduction* or *natural transformation*. At present it is not clear which components of IM participate actively in these mechanisms (Modi, SR 2014).

Antibiotics have a special role in the development and increase the gut resistance gene reservoir. It is estimated that, in the developed countries, 1-3% of the population follows treatments with AB in daily life (Modi, SR, 2014).

Antimicrobial drugs tend to facilitate the transfer of gene information, including exchanges of microbial interspecies variation of multidrug encoding DNA components. Also, with antibiotics, phages mobility increases.

In addition, IM structure perturbation through the ABs open niches for new resistant germs. In the context of ABs use, the presence of pathogenic and comensale microbial consortia in the gut offers an opportunity for transfer of resistance genes to virulent species (Modi, SR 2014).

Not only administration of ABs to the patients is responsible for the emergence and dissemination of the resistors. Genes of resistance to ABs are widespread in the environment. The use of ABs in animal husbandry, agriculture or aquaculture allows that, along with food, to enter into the human body minimum doses of drugs, non-noxious for the host but sufficient to produce new microbiom resistors.

 DOI: 10.12865/CHSJ.42.03.12

COLONISATION BY GERMS MULTURESISTANT TO ANTIMCROBIALS, KEY FACTOR PRECEDING THE INFECTION IN THE INTENSIVE CARE UNIT

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English abstract not available.

ADVANTAGES AND LIMITS OF MACROLIDES IN TREATING COMMUNITY-ACQUIRED PNEUMONIA IN HOSPITALIZED PATIENTS

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Advantages of macrolides when treating community-acquired pneumonia (CAP) are related to their activity on atypical organisms and their immunomodulatory and anti-inflammatory properties, which may result in a decrease of mortality. Initial antibiotic treatment of CAP is largely empirical. Major guidelines recommend in general, an antibiotic regimen covering both typical and atypical pathogens in hospitalized CAP patients, but the necessity of the atypical coverage has not been proven in a recently published Cochrane review. Studies comparing mortality with betalactam/macrolide-based regimen vs betalactam alone are lacking, most studies compare betalactam/macrolide with a fluoroquinolone regimen. The results of a recent meta-analysis suggest a benefit for macrolide-based treatment, but analyses restricted to randomized clinical trials (RCT) or to patients who received guideline-concordant regimens (with substantially less heterogeneity than in the overall analysis) show a reduced difference. On the other hand, it has been suggested that the use of macrolides is associated with an increased risk of mortality due to cardiovascular events, but this risk might have been overestimated, since the large majority of subjects experiencing cardiac arrhythmias from macrolides have coexisting risk factors and the incidence of arrhythmias in absence of coexisting risk factors is very low. Older age is one of the risk factors of cardiovascular complications in patients hospitalized with CAP. In conclusion, macrolides can be safely used in the majority of subjects for whom they are recommended, although RCT comparing mortality of a betalactam/macrolide-based regimen vs betalactam alone are necessary to support the decrease of the mortality with the macrolide-based regimen.

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INFECTIONS IN IMMUNODEPRESSED PATIENTS: THERAPEUTICAL OPTIONS UPDATE

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Patients with immunity abnormalities or treated with corticosteroids or immunosuppressive therapies have a high risc to develop infections with opportunistic germes, and some viral and fungal infections could significantly affect associated morbidity and mortality. Essential points regarding antiinfective therapy in immunodepressed/neutropenic patients rely on choosing the best antimicrobial or antifungal therapy, determining the optim duration and choosing an alternative regimen. In choosing an antimicrobial regimen must be taken into account the following factors: local antibacterial epidemiology and resistance patterns, patient's prior colonization or infection with a resistant pathogen (particularly MRSA with vancomycin MIC> 2mg/l, vancomycin-resistant enterococci, ESBL or carbapenemase producer - enterobacteriaceae , *A. baumanii, P. aeruginosa, Klebsiella pn.* carbapenem- resistant, *S. maltophilia*), other patient-related factors (ex. severity of the disese, risk factors for infections with resistant pathogens), an escalation type therapy or a de-escalation formula. Classical escalation therapy with third generation cephalosporins or piperacillin- tazobactam is still a good option in many services but requires a strict surveillance. De-escalation therapy starting with carbapenems or some agressive anti-KPC combinations might be recommendable depending on local epidemiology or patient condition. Invasive fungal infections remain a serious threat for patients with persistent neutropenia, with an associated mortality of 40-75%. Therapy management with initial antifungal empirical treatment or a targeted , diagnostic based – therapy is still a subject of debate regarding the rate of succes.

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RESISTANCE OF HEPATITIS C VIRUS TO DIRECT ACTING ANTIVIRAL DRUGS (DAA)

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English abstract not available.

ANTIVIRAL THERAPY IN INFECTIONS DUE TO HERPESVIRUSES – RESISTANCE TO ANTI-HERPECTIC AGENTS A THREAT IN 2015?

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English abstract not available.

MOLECULAR MECHANISMS OF INFLUENZA VIRUS RESISTANCE TO NEURAMINIDASE INHIBITORS - A REWIEW

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Influenza A and B viruses are the most common human respiratory viruses. The hemaglutinine/ HA of influenza A and B viruses binds to neuraminic acid-containing receptors of host-cell . The neuraminidase (NA) enzymatic activity promotes influenza virus infection by blocking the enzyme active site. There are two major classes of antivirals available for the treatment and prevention of influenza, the protein - M2 inhibitors and the neuraminidase inhibitors (NAIs). The M2 inhibitors are only effective against influenza A viruses, and resistance arises rapidly. There are four NAIs licensed in some parts of the world, zanamivir, oseltamivir, peramivir, and a long-acting NAI, laninamivir. The current influenza A H3N2 and pandemic A(H1N1)pdm09 viruses, are already resistant to the matricial M2 inhibitors as are many H5N1 viruses. Decreased susceptibility to NAIs can occur as a result of mutations at the conserved residues in the active site of NA, which can limit the interaction of the drug with the sialic acid binding pocket of NA (NA-dependent resistance). Previous studies have shown that resistance to NAIs varies with the NA subtype of influenza virus and that distinct NA mutations may cause different patterns of resistance. Four major mutations in NA that can cause NAI resistance have been reported. In influenza viruses of the N2 subtype, a glutamic acid to valine substitution in residue 119 (E119V, N2) confers resistance to oseltamivir but not to zanamivir; An arginine to lysine substitution at position 292 (R292K) confers resistance to both NAIs. Most H1N1 viruses circulating since the 2007-2014 influenza season have a histidine to tyrosine substitution at residue 274 (H274Y), which is also associated with resistance to oseltamivir but not zanamivir . Other mutations such as an asparagine to serine substitution at position 294 (N294S), have been reported in both N2- and N1-containing viruses; these mutations are associated with a greater loss of in vitro susceptibility to oseltamivir in N2 than in N1 viruses but strains possessing these mutations retain susceptibility to zanamivir . E119V and N294S mutations occur in the framework region of the NA. Resistance to the second class of anti-influenza drugs, Adamantanes, results in most cases from a single serine to asparagine amino acid replacement (S31N) in the matrix M2 protein, which can interfere with the drug's ability to block M2 ion channel activity and viral replication . Our review focuses on resistance to the NAIs.

ANTIRETROVIRAL RESISTENCE – THEORTIC AND PRACTIC APROACHES

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Human immunodeficiency virus (HIV) after infecting host cells multiplies rapidly and subsequently is characterized by the existence of multiple viral quasispecii. Some of them are not viable, but define viral polymorphism (heterogeneous viral population). Thus even in the absence of antiretroviral medications genetic mutations may occur (primary resistance in naïve patients). Primary resistance also can be seen through vertical transmission (from mother to child) or horizontally.

Rate of HIV-1 replication is 10.3×10^{9}virioni / day and half-life of free viral particles in the plasma is of up to 6 hours. Turn-over (generation time) of HIV-1 is 1.8 days (defined as the time from the release of a virion until it infects another cell and release a new generation of viral particles). HIV-1 genome consists of 10^4 base pairs and the rate of occurrence of mutations in HIV-1este estimated at 3.4×10^5 / pair base / round of replication. So any mutation in any position in the genome can defend even repeated every day. It is known fact that mutations occur more rapidly at high viremia (at a viral load of 300.000copii / ml mutations occur in 1 day, at viral load of 300 copies/ml mutations occur in 100 days)

 DOI: 10.12865/CHSJ.42.03.12

In the presence of antiretroviral medication, when given the correct combination therapy, the virus can no longer multiply and therefore viral mutations no longer appear. When treatment is administered incorrectly (dose, drug interactions, impaired absorption, adherence, etc.) virus starts multiplying again and resistance mutations appear, this time drug-resistant mutations (selected secondary drug resistance). Minor mutations have been identified that "per se" do not cause major viral resistance mutations, indicating viral resistance to a particular drug, to a certain class of drug or cross-resistance between different classes of antiretroviral drugs.

Genetic barrier to resistance describes the number of mutations required for a drug to lose activity or how difficult it is to acquire a drug-resistance mutations. NNRTIs have low genetic barrier, in a single step (single mutation, ie. K103N, makes the virus resistant to EFV and NVP) and PI/r have high genetic barrier, in several steps, ie PI/r need more mutations (3-6) for the virus to be resistant to these drugs.

Currently there are many kinds of resistance tests: genotype, phenotype, "virtual" phenotype and sensitive assay for detection of low frecvency mutation. Genotypic resistance tests are those types of tests that identify changes in viral sequences known to be associated with resistance (molecular). Phenotypic resistance tests measure the capacity for HIV-1 growth in the presence of individual drugs – (biological)."Virtual" phenotype use genotype results to predict phenotypic susceptibility based originally on database of paired genotype and phenotype data or, more recently, through scores derived from linear regression analysis. Detection of low frecvency mutations are useful in identifying resistance mutations not detected by the standard assays before therapy

NON-ANTIBIOTIC EFFECTS OF MACROLIDES AND THEIR ROLE IN THE CURRENT MANAGEMENT OF LOWER RESPIRATORY TRACT INFECTIONS

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Respiratory tract infections (RTI) represent worldwide a major health problem, associated with high morbidity and mortality and the main reason for prescribing antibiotics. In the past decades, a constant increase of antibiotic resistance in pneumococci has been recorded, leading to additional increase in mortality and difficulties in choosing the right antibiotic therapy. The appropriate antibiotic for RTI should have a narrow spectrum, covering the most frequent bacteria involved in RTI: S. pneumoniae, Haemophillus spp., Moraxella spp, M. pneumoniae, C. pneumoniae and L. pneumophila. The antibiotic class with the most adequate spectrum for RTI and also with good penetration in the alveolar fluid are macrolides (erythromycin, clarithromycin, azithromycin and josamycin). Besides their antibiotic effect, macrolides also have anti-inflammatory, immunoregulatory and mucoregulatory effects, leading to high clinical and antibacterial success rate, when compared to other antibiotic classes. The non-antibiotic effects of macrolides consist in: ciliary epithelium protection, stimulating mucociliary clearance, inhibition of inflammatory mediators release: IL8, TNF-alfa, nitric oxide, inhibition of adhesion molecules expression ICAM-1, endothelin-1 and defensins, reducing the adhesion of pneumococcus to the respiratory epithelium, inhibitting quorum sensing, biofilm production and pneumolysin synthesis. These non-antibiotic effects were demonstrated on patiens with COPD exacerbations, cystic fibrosis and chronic sinusitis. The immunomodulatory and anti-inflammatory effects prooved to be beneficial in bacterial superinfection of influenza, significantly lowering the mortality rate when compared to other antibiotic classes. For all these reasons, current guidelines (IDSA/ATS-2007, BTS 2009, The Stanford Guide 2012, Pilly 2014) recommend the use of macrolides, especially clarithromycin as a first choice antibiotic in uncomplicated community acquired pneumonia, in patients without comorbidities or risk factors for antibiotic resistance. Hospitalization is recommended in severe pneumonia, patients with comorbidities or risk for antibiotic resistance. The first choice antibiotic recommended in hospitalized pneumonia is either respiratory quinolone monotherapy (moxifloxacin or levofloxacin), or a betalactam-macrolide association (amoxicillin/clavulanate or ceftriaxone + clarithromycin). Macrolides, especially clarithromycin remains one of the main choices for RTI treatment.

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BACTERIAL ANTIBIORESISTANCE, MEDICAL ISSUES, SOCIAL AND ECONOMIC "PRESENT AND FUTURE"

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Bacteria are present on Earth over 3.5 billion years and modern man for no more than 150,000 years.

More than 50% of the Earth's biomass is represented of bacteria out of which only 5% have been found and classified.1 g of soil contains between tens of thousands and millions more bacterial species. Every man and animal on the planet harbors billions of bacteria. The number of bacteria in humans is 10 times higher than the number of cells. (1000-1500 g of bacteria, most of the digestive tract). 1 g of saliva contains 1 billion bacteria and 1 g of feces 100 billion.

Bacterial resistance to antibiotics is a natural phenomenon that appeared long before man discovered and used antibiotics in medical practice. Many antibiotics are produced by the bacteria itself. Antibiotics of the bacterial secretion aim to eliminate other bacteria competing in the environment. Bacteria that produce antibiotics develop concomitant enzymes that protect them for antibacterial substances. By transfer between bacteria, the genes coding for these enzymes resistance are transmitted to other species that in turn become resistant to antibiotics.

This natural process has increased enormously in recent decades due to:

a) the discovery and use of antibiotics in human and veterinary medicine (treatment, prophylaxis) in animal husbandry and aquaculture (growth factor), agriculture (treatment of bacterial diseases of fruit trees, flowers, vegetables), industry (industrial paints).

b) Massive use of industrial and householdbiocides, similar or even identical with some antibiotics.

c) Utilization of disinfectants in hospitals and at home.

d) Intensification of the movement of resistant bacteria strains in nature, animals and humans, and between animals and humans.

Over 50% of the antibiotics produced in the world are intended for veterinary use (≈ 27,000 tons)

In the US in 201117,100 tons of antibiotics were sold out of which 3,500 tons for human use (20.5%) and 13,600 tons for veterinary use (79.5%). In Europe (29 countries)3350 tons of antibiotics have been used in human medicine in 2007.

World consumption of antibiotics has increased by about 40% between 2000 and 2010.

Consumption of antibiotics in Europe -2012 (ESAC-Net) averaged 21.5 DDD / 1000 inhabitants / day; the lowest consumption in Northern Europe (Scandinavia and the Baltic countries), the highest consumption in Greece and Romania (> 19.6 DDD / 1000 inhabitants / day). Consumption of cephalosporins III-rd generation of the EU: 1.7- 1.9 DDD / 1000 inhabitants / day compared to RO: ≈ 5.2 DDD / 1000 inhabitants / day (overall consumption in the community and hospital). EU consumption of ciprofloxacin in 2012: 0.35 DDD / 1000 inhabitants / day in the UK., 1.7 DDD / 1000 inhabitants / day in Luxembourg and ≈ 3.5 DDD / 1000 inhabitants / day in Romania.

40% of antibiotics prescribed by doctors are not required (WHO).

Antibiotic resistance is now a serious public health threat. It is present and growing both to "common" antibiotics and to those of the "reserve". The world is moving towards post antibiotic era where current infections could kill us again. (WHO 2014).

The rapid development of bacterial resistance in the world is "a very real and disturbing threat that could restore the medieval world of medicine deaths caused by infections that can be cured today." (David Cameron, 2014)

Antibiotic-resistant bacteria are causing now a minimum of 700 000 death/ year in the world, of which 27,000 in Europe and 23,000 in the US.

Further increase of the resistance of bacteria to antibiotics will cause by 2050 300 million deaths (10 million deaths / year), causing an erosion of global GDP by 2-3.5%. Of the 10 million deaths / year, most will occur in Asia (4.7 million) and Africa (4.1 million) and less in Europe (390,000) and the United States (317,000).

By 2050 deaths by infections by resistant bacteria will become the first cause of death in the world, ahead of cancer (8.2 million deaths / year), diabetes (1.5 million), diarrheal disease (1.4 million) or car accidents (1.2 million). The economic cost of infections caused by bacteria

 DOI: 10.12865/CHSJ.42.03.12

antibiotic residence will be in the next 35 years, in the world, of between 60-100 trillion.
In the US overall cost of hospital infections caused by antibiotic-resistant bacteria is over $ 20 billion / year.
In Europe in the last four years, the percentage of antibiotic resistant bacterial strains including third generation cephalosporins and carbapenems has increased significantly.
The same situation is in Romania where, according to national report on antibiotic consumption and resistance in 2012 "bacterial resistance is at an extremely highdue to exaggerated and erroneous use of antibiotics".
In the last 10 years very few new antibiotics have been introduced in therapy, as international laboratories practically abandoned research on antibiotics, mainly due to economic reasons.
Today we are witnessing a growing imbalance between the decreasing number of new antibiotics for clinical use and the acceleratednumber of bacterial resistance, which makes the risk of therapeutic impasse to become more frequent.
In order to cope with this situation it is important to find a solution that can prevent the emergence of resistance, because bacteria will always find a way to adapt, but rather preserve for as long as we can the effectiveness of available antibiotics.

ANTIBIOTIC MANAGEMENT PERCEPTION IN ROMANIA (MULTIREGIONAL STUDY)

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English abstract not available.

SUBSTANTIATION AND GUIDELINES FOR AN ANTIBIOTIC STEWARDSHIP PROGRAMME IN ROMANIA

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English abstract not available.

NON-ABSORBABLE ANTIBIOTICS AND THEIR PLACE IN THE ACTUAL TREATMENT OF ACUTE INFECTIOUS DIARRHEA

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In developing countries acute diarrheic disease remains a major problem of public health, being responsable for 25% of deaths recorded in children under 5 years. The explosive growth in the last years of the number of turists that travel in countries with low levels of hygene has led to the growth of traveler's diarrhea incidence, which affects 40% of the travelers. Dramatic expansion of antibiotic use in the last years, especially betalactamins and fluoroquinolones, determined an important increase in the postantibiotic diarrhea incidance rate. In present there is a worldwide concern about the dramatic increase in the incidance rate of diarrhea caused by *Clostridium difficile*, therefore international scientific societies of infectious Diseases and Gastroenterology are looking for new therapeutic strategies for prevention and control of this pathology. Acute diarrheic syndrome's therapeutic principles consist of hydroelectolitic rebalancing, systemic antibiotherapy or non-absorbable antibiotics and sparing diet. Actually, alfa-rifaximin has a priviledged place among non-absorbable antibiotics due to its large antibacterial spectrum, low risk of selecting resistant strains and it's good tolerability. Comparative studies of systemic vs non-absorbable antibiotics showed non-inferiority or even superiority of alfa-rifaximin in treatment of mild and medium forms of intestinal infections. Severe forms of disease require reference to a specialist physician for inhospital surveillance and adequate systemic antibiotherapy. Non-absorbable antibiotics are now considered by the International Society of Travel Medicine and FDA as the first choice for prevention and treatment of traveler's diarrhea. Non-absorbable antibiotics used after the end of the standard treatment with Vancomycin or Metronidazole po in diarrheas caused by *Clostridium difficile* have proved to be efficient in prevention of relapse. Non-absorbable antibiotics represent an efficient therapeutic solution and sometimes the only one for some forms of acute infectious diarrhea.
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KNOWLEDGE, OPINIONS AND ATITUDES ON ANTIBIOTIC CONSUMPTION IN "DUNAREA DE JOS" UNIVERSITY FROM GALATI

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Background: antibiotic resistance is a worrying phenomenon worldwide. Prudent use of

antibiotics in European Union (EU) is encouraged during educational programs for health workers and general population . " Eurobarometer survey " reports the data on the knowledge, opinion and behavior on antibiotic use in 28 EU states. **Objective**: assessment of the opinions and knowledge on antibiotics of medical students from "Dunarea de Jos" University Galati. **Material and method**: this cross-sectional study used Self-reported questionnaire method. Responses were statistically analyzed and compared with data of " Eurobarometer survey ". **Results**: there were 182 participants, aged between 24 and 34 years, 84 % female. In the past 12 months, 66 % used one or more antibiotics, but 31% did not have a prescription. The most common cause of antibiotic use was dysphagia. About the questions on antibiotic knowledge, 71% of answers were correct. 62% of participants are aware that each of us influence the effectiveness of antibiotics. Similar to other EU states and national data, the most important source of information on antibiotics is the doctor (88.5%). Students inform themselves on the internet (41%), magazines, encyclopedias and medical journals (42%). The level of knowledge on antibiotics correlates with the information source medical journals ($p = 0.032$) and with the use of antibiotics by prescription ($p=0.022$). **Conclusion**: students are better informed on antibiotics use in comparison with the general population, but their knowledge does not concur with their attitude. Health policies should promote the practical application of medical knowledge.

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STREPTOCOCCUS PNEUMONIAE SUSCEPTIBILITY TO ANTIBIOTICS

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Introduction: antibiotic therapy is the key to successful treatment, which is why is needed a constant monitoring of antibiotic sensitivity of the involved bacteria. **Objectives**: *Streptococcus pneumoniae*'s phenotype analysis of antibiotics sensitivity at the HIV seronegative adults. **Material and method**: retrospective and comparative study between the period 2007-2010 and 2011-2014, realised in Infectious Diseases Hospital of Craiova, on the evolution of *Str.pneumoniae*'s sensitivity. There were considered multiresistant strains those that showed resistance of at least 3 different antibiotics. Differences were considered statistically significant for a threshold of $p <0.05$ and the regression coefficient (R). **Results**: in 2007-2010, there were 234 strains identified of *Str.pneumoniae* with the following rate sensitivity: ceftriaxone 84.61%, moxifloxacin 97.43% , linezolid 97.43%, trimethoprim-sulfamethoxazole 50.84%, vancomycin, 97.43%, erythromycin 70.94%, rifampicin 92.73%, penicillin 39.31%, teicoplanin 100%. In the period 2011-2014 there were identified 327 Str.pneumoniae strains, with the following ratio of sensitivity to antibiotics: ceftriaxone 44.26%, cefotaxime 96.55%, ceftaroline 100%, ofloxacin 91. 97%, moxifloxacin 100%, oxacillin 30.67%, linezolid 96.3%, chloramphenicol 86.15%, trimethoprim-sulfamethoxazole 68.66%, vancomycin 95.31%, clarithromycin 84.76%, ertapenem 47.62%, clindamycin 81.33%, rifampin 95.45%, tetracycline 44.44%. The sensitivity evolution of *Str. pneumoniae* to ceftriaxone recorded a downward trend ($R^2 = 1$), and at trimethoprim-sulfamethoxazole an ascending one ($R^2 = 1$). Multiresistant strains were observed in 61 cases (18.66%) in 2011-2014 versus 23 cases (9.83%) in 2007-2010; $p = 0.0039$. **Conclusion**: there were registered the following changes in the phenotype of sensitivity to antibiotics of *Str. pneumoniae*: reduction of sensitivity to ceftriaxone, increasing of trimethoprim-sulfamethoxazole,and the high risk of multiresistent *Str. pneumoniae* in the 2nd period of the study. The sensitivity to vancomycin, linezolid, moxifloxacin, rifampicin was maintained increased and average for macrolide (erythromycin, clarithromycin).

Keywords: antibiotic, *Streptococcus pneumoniae*, sensitivity

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ANTIMICROBIAL RESISTANCE AND ISOLATED *SHIGELLA* SEROGROUPS IN HOSPITALIZED PATIENTS FROM THE INFECTIOUS DISEASES CLINIC CRAIOVA

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 DOI: 10.12865/CHSJ.42.03.12

Shigella spp. shows regional particularities that require data updating regarding circulating strains and their sensitivity to antibiotics. **Objectives**: the study followed the distribution of *Shigella* serogroups and the antibiotic resistance profile at the Dolj county level in order to target therapeutic choices. **Material and methods**: 511 *Shigella* strains isolated from coprocultures of hospitalized patients at the Infectious Diseases Clinic between 2001 -2014 Craiova were studied retrospectively. The serogroups were determined by standard method and the chemosensitivity by antibiogram diffusion. Chi^2 test was used to compare the chemoresistance of different samples ($p < 0.05$ as statistically significant). **Results**: 78.7% of cases were pediatric, the most affected age group was 0-4 years (47.7%). The serogroups' distribution was: *Shigella flexneri* (78.08%), *Shigella sonnei* (17.4%), *Shigella boydii* (2.93%) and *Shigella dysenteriae* (1.56%). The chemosensitivity of the tested strains was: Ampicillin 30.2 %, Tetracycline 40.85% , Trimethoprim sulfamethoxazole 58.4%, Ceftriaxone 83.6%, Ciprofloxacin 89.85%, Gentamicin 91.3%, Colistin 92.5%, Meropenem 100%, Cefixime 100%. During the analyzed period, there was a statistically significantly decreased chemosensitivity of *Shigella* to ampicillin (45.2% to 20%), Trimethoprim sulfamethoxazole (65.3% to 45.4%) and Ceftriaxone (87.5% to 78.5%). The decrease of chemosensitivity was not significant to Tetracycline (46.3% to 40%) and Ciprofloxacin (92.5% to 88.8%). The sensitivity to Colistin had increased (86.4% to 100%) with the absence of chemoresistance to Meropenem.
Shigella dysenteriae presented a higher chemoresistance compared to other serogroups. **Conclusions**: *Shigella flexneri* is the most common regional serogroup. Increased chemoresistance to Ampicillin, Tetracycline and Trimethoprim sulfamethoxazole restricts their use in therapy. Fluoroquinolones, Cephalosporins, Colistin are therapeutically effective. **Keywords**: *Shigella*, serogroup, chemoresistance
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ANTIBIOTICS SUSCEPTIBILITY OF GERMS ISOLATED IN PATIENTS DIAGNOSED WITH URINARY TRACT INFECTIONS

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Objectives: Analysis of the incidence, etiological specter in urinary tract infections and antibiotic susceptibility of germs isolated from urine samples. **Methods**: Retrospective study (01.Jan.2013-31.Dec.2013) in 2 groups of adult patients (Pt) which were hospitalized in "Victor Babes" Hospital of Infectious Diseases and Pneumology- Craiova: group A has 219 HIV-infected patients, group B-4848 HIV uninfected Pt. From the two groups were compared and analyzed the isolated strains from urine samples, while the antibiogram was performed by standard diffusion method. Statistical significance was assessed by calculating RR and p, using the Fischer test. **Results:** The incidence of urinary tract infections: 33 Pt (15.1%) in group A vs 352 Pt (7.3%) in group B ($1.27 < RR = 2.07 < 2.88$, $p < 0.005$). Etiology was represented in group A by *Escherichia coli* (*E. coli)* (24), *Enterobacter spp*. (4), *Klebsiella pneumoniae* (*Klebsiella pn.)* (3), *Proteus* (2) and from the group B there have been isolated strains of *E. coli* (248), *Enterobacter spp* (18), *Klebsiella pn* (61), *Proteus* (15), *Pseudomonas aeruginosa* (5), *Citrobacter* (5). Recurrent urinary infections had been identified in 3 Pt from group A and 6 Pt from group B. Urosepsis was present at 5 Pt (2.29%) from group A vs 48 Pt (0.9%) in group B ($0.16 < RR = 2.3 < 4.45$, $p < 0.005$. Antibiotic sensitivity of *E. coli* strains in group A: cefaclor-57.14%, cefuroxime-72.22%, piperacilina/tazobactam-93.1%, norfloxacin-92%, nalidixic acid- 84.62%, trimetoprim/ sulfametoxazol-60.87%, ceftriaxone-90%, meropenem 100%, colistin -93.3%, gentamicin-83.33%, ampicillin/sulbactam-58.62%, ampicillin-23.07%, imipenem-100% vs group B: cefaclor-58.46%, cefuroxime-74.79%, piperacillin/tazobactam-83.27%, norfloxacin-72.58%, nalidixic acid- 67.4% trimetoprim/sulfametoxazol-58.24%, ceftriaxone-76.16%, meropenem-98.76%, colistin-76.83%, gentamicin-79.89%,, ampicillin/sulbactam-63.03% ampicillin - 30.55% imipenem-95.45%. Antibiotic sensitivity of *Enterobacter* strains in group B:

cefaclor-25%, cefuroxime-39.29%, piperacilina/tazobactam-58.82%, norfloxacin-72.22% trimetoprim/sulfametoxazol-42.86%, ceftriaxone-66.6%, meropenem-83.33%, colistin-81.25 %,gentamicin-64.28%, ampicillin/sulbactam-63.63%, ampicillin-62.5%; imipenem-91.66%. Antibiotic sensitivity of *Klebsiella* strains in group B: cefaclor-33.33%, cefuroxime-37.93%, piperacilina/tazobactam-52.46%, norfloxacin -62.30%, nalidixic acid - 66.66% trimetoprim/sulfametoxazol-35.41% ceftriaxone-51.16%, meropenem-80.95%, colistin-75.86%, gentamicin-66.66%, ampicillin/sulbactam-31.58%, ampicillin-0%.**Conclusions**: HIV-infected patients have an increased risk of developing urinary tract infections and urosepsis. The etiology of urinary tract infections is dominated by *E. coli* both in HIV infected Pt, as well as HIV uninfected Pt; there is a decreased susceptibility to ampicillin, second generation cephalosporins, trimethoprim /sulfamethoxazole for uropathogenic strains.

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MICROBIAL RESISTANCE TO ANTIBIOTICS IN INTENSIVE CARE CLINIC II TG MURES

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Introduction. Critically ill patients admitted to the intensive care units (ICU) are exposed to hospital acquired infection with extended resistant (R) germs. **Objective:** study the resistance of germs isolated from a mixed ICU (surgical and medical) patients. **Material and method**: we performed a cross-sectional, retrospective study at the Intensive Care Clinic II Tg.Mures in 2013-2014. We analyzed 226 germs (isolated from 160 patients). Statistical analysis was performed with Fisher's exact test, with significance threshold of $p < 0.05$. **Results**: 137 germs were Gram-negative (GN), 89 Gram positive (GP). Of GN prevailed: 1, *Acinetobacter* spp, 38 strains (s), from oro-tracheal canulla 24s (otc), 34R to imipenem, 32R to cefepime, 23R to amikacin, 0R to colistin; 2, *Pseudomonas aeruginosa*, 36s, 20s of the otc, 21R to ceftazidime, 20R to tobramycin, 19R to imipenem, 4R to ciprofloxacin, 0R to colistin; 3, *Klebsiella pneumoniae* 24s, 10s from oct, 21R to clavulanic acid-amoxicillin, 20R to ciprofloxacin, 20R to cefuroxime-axetil, 5R to sulfamethoxazole trimethoprim. Among GP prevailed: 1, methicillin-resistant *Staphylococcus* 37s, 13s from otc and 14 from cutaneous wounds (cw), 34R to erythromycin, 33R clindamycin, 24R to levofloxacin, 3R to linezolid, 0R to vancomycin; 2, *Enterococcus* spp., 22s, 3s from otc, 14s from cw, 2R to clindamycin, 0R to linezolid, 0R to vancomycin. From otc predominantly GN were isolated, and from cw mostly GP (p:0,0001). **Conclusions**: GN germs were R to the most commonly used antibiotics in the ICU, like carbapenems, cephalosporins, fluoroqinolones, aminoglycosides. Colistin and vancomycin were useful. GN prevails in intubated patients.

Keywords: resistance, antibiotics, intensive care

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A COMPARATIVE STUDY ABOUT THE ANTIBIOTIC RESISTANCE OF *KLEBSIELLA* STRAINS FROM INTENSIVE CARE UNIT

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Introduction: *Klebsiella* infections are common in Intensive Care Unit (ICU) wards in patients with multiple pathologies. **Objectives:** evaluation of *Klebsiella* infections prevalence in ICU ward and antibiotic resistance profiling. **Material and methods:** this cross-sectional study included 930 patients febrile with respiratory clinical symptoms and purulent collections hospitalized in the ICU ward of Clinical Emergency County Hospital, Craiova, Romania. We collected tracheobronchial secretions and purulent. The specimens were subjected to classical bacteriological diagnosis (CLSI 2014). **Results:** *Klebsiella* strains from tracheobronchial secretions (24%) vis-a-vis purulent secretions (42.50%) were resistant in high percentages at: ticarcillin with clavulanic acid (100%), aztreonam (57.6% vs. 30%), ertapenem (51.5% vs. 50%), ciprofloxacine (36% vs. 40%). Low resistance was observed to amikacin 10.7% vs. 11.10%) and cefoperazone with sulbactam (7.1% vs. 10%). Strains isolated from tracheobronchial secretions were significantly more resistant (resistance index = 71% vs. 59%) and particularly to aztreonam (Risk Ratio (RR) = 1.92) 4th generation cephalosporins - cefepime (RR = 1.67) and 3th

 DOI: 10.12865/CHSJ.42.03.12

generation cephalosporins - ceftriaxone (RR = 1.45). There were no significant differences of resistance to ceftazidime, cefazolin, cefoperazone with sulbactam, amikacin and ciprofloxacin. Strains isolated from tracheobronchial secretions showed MDR in 48.57% of cases, the most common phenotypes were: TZP-CIP-CXM, AMK-GEN-CIP-CXM, AMK-AMC-TZP-CIP-CXM and AMC-AMK-GEN-CIP-TZP-CXM. Strains isolated from purulent secretions were less resistant (33.33% - MDR), mostly were just resistant to 3 antibiotics (TZP-CIP-CXM) and only 8.33% to 6 antibiotics (AMK-AMC-GEN-TZP -CIP-CXM). **Conclusions:** these antibiotic resistance differences suggest a greater involvement of MDR *Klebsiella* strains in lower respiratory tract infections.

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EXTENSIVE STUDY ON RESISTANCE OF GRAM NEGATIVE BACILLI ISOLATED IN COUNTY HOSPITAL ARAD

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Introduction: the rise in incidence of Gram negative strains isolated in urinary infections, requires periodic evaluation of antibiotic resistance for instituting anefficient antibiotherapy. **Objectives:** study of antibiotic resistance of gram negative bacilli isolated in county hospital Arad in 2014, identification of ESBL phenotypes (extended spectrum beta lactamase producing)and fluoroquinolone resistant phenotypes. **Material and method**: We analysed 520 Gram negative bacilli positive urocultures.An etiologic diagnosis was made by isolating Gram negative bacilli in aerobic cultures in cromogenic medium, optical microscopy, miniAPI system.We used difusometric method respecting CLSI2010 standards, for identifying resistant phenotypes and specific synergy test (champagne cork)for ESBL's. **Results**: most frequently isolated was Escherichia (E.) coli- 69,42 % (361 cases), Proteus mirabilis - 7,88% (41), Klebsiella pneumoniae - 5,96 % (31), Pseudomonas aeruginosa - 3,84% (21), Enterobacter aerogenes - 4,42% (23), E. hermanii - 3,84% (20), Citrobacter freundii - 1,34% (7), Klebsiella oxytoca - 1,73% (9), Acinetobacter baumannii - 0,76% (4), Morganella morganii - 0,57% (3). Resistance to antibiotics varied. We iolated 54 ESBL strains (14,95%) for E.coli and 39 fluoroquinolne resistant phenotype IV strains (10,80%). For Proteus mirabilis – 20 ESBL strains (48,78%) and 7 – fluoroquinolone resistant (17,07%); Klebsiella pneumoniae - 19 ESLB's(61,29%) and 11- fluoroquinolone resistant (35,48%). For other Gram negative bacilli– 17 strains of ESBL's and 8-fluoroquinolone resistant strains. **Conclusions:** a large number multiple resistance strains of Gram negative bacilli is observed. We observed a high frequency of ESBL strains. **Key words:** bacilli, ESBL,quinolones.

STAPHILOCOCCAL INFECTION IN IV DRUG USERS HIV SEROPOSITIVE

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Background: infection with *Staphyloccocus aureus* (S.A.) is the most common bacterial infection of the infected HIV intravenous drug users (IDUs). S. A. is the leading cause skin infections but also those causing death-endocarditis, sepsis. **Aims**: to analyze the clinic and treatment of HIV + IDUs infected with S.A in the period 2013- 2014 in Adult HIV / AIDS Department of our hospital. **Material and method**: retrospective and prospective study of S.A. infections. MSSA / MRSA in 31 of 139 patients hospitalized during this period in our Department. HIV diagnoses and identify S.A. were carried out by conventional techniques. **Results:** S.A. infections had 22.30% of patients. Skin infections had 62%, followed by 22 % pulmonary and 10% systemic. Infections. MRSA isolates,were 35% of S.A, regardless of the type of drug use (heroin and / or ethnobotanical drug), but depending on the duration dependence (> 5 years). S. A. was resistant to penicillin G (95.9%), erythromycin, tetracycline, clindamycin .. MRSA strains were sensitive to vancomycin in 100% cases and gentamicin too. Treatment of choice was ceftiaxona associated with ciprofloxacin. There were 17, 5% deaths Antiretroviral therapy started. 38% of patients but nonaderenta was dominant. Coinfected TB were in 56% patients **Conclusion**s: the use of disposable needles and syringes, injection facilities and opiate substitution programs can reduce the incidence of infection. **Keywords**: iv drug use, HIV infection, staphylococcal infection.

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INFECTIVE ENDOCARDITIS - EVALUATION OF CLINICAL FEATURES, CAUSATIVE AGENTS AND OUTCOME IN A TERTIARY FACILITY

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Objectives: infective endocarditis (IE) is a challenging diseases with poor prognostic and high mortality. The aim of our study was to evaluate epidemiology, clinical aspects, aetiology and outcome of IE hospitalized in out hospital. **Material and methods:** we conducted a retrospective analysis of patients diagnosed with IE (Duke's criteria) and admitted between January 2012 – July 2014 in Clinical Hospital of Infectious and Tropical Diseases Dr Victor Babes Bucharest. **Results:**117 patients were included (78 men). The age range was 11-84 years. 88 patients (75,2%) were transferred from other hospitals for specialist care and 29 (24,8%) were admitted directly from the community. Valve involvement : aortic 51, mitral 41, tricuspid 5, pulmonary 1 and more than 1 valve in 19 cases. Most cases 95 (81,2%) had native valve endocarditis and only 22 had IE of a prosthetic valve. 75 (64,1%) were known with a preexisting valvulopathy. All patients had an echocardiogram. Blood cultures were positive for 61 patients (52,1%) and 59 (50,4%) received antibiotic treatment before admission. *Staphylococcus epidermidis* was isolate in 19 cases (31,1%) 6 methicillin-resistant followed by *Streptococcus viridans* 17 (27,8%), *Staphylococcus aureus* 11 (18%) 4 methicillin resistant, *Enterococcus spp* 8 (13,1%), *Granulicatela elegans* 2 cases and one case each with *Escherichia coli, Pseudomonas aeruginosa, Sphingomonas paucimobilis* or *Propionibacterium bacteroides fragilis*. Cardiothoracic surgery valve replacement was performed for 53 patients (45,2%). 84 patients (71,8%) had one or more complications due to IE and treatment adverse events. Major embolic complications included stroke 16 cases (13,7%), embolization other than stroke 12 (10,3%). 95 (81,2%) patients had a good outcome and 22 (18,8%) died.**Conclusions:** patients were especially elderly. The most frequent isolated bacteria was *Staphylococcus spp*, followed by *Streptococcus viridans* and *Enterococcus spp*. IE requires a multidisciplinary stewardship because is a severe diseases with high mortality and high complications rate. **Keywords**: infective endocarditis, *Streptococcus viridans, Staphylococcus aureus,* embolization

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THERAPEUTIC ASPECTS IN SEPSIS WITH GRAM-POSITIVE ETIOLOGIC AGENTS

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The considerable increase of the resistance to antibiotics of Gram-positive bacteria, and in particular *Staphylococcus aureus* in the past 20 years, with the development of methicillin resistance, has been recently accompanied by a decrease in sensitivity to Vancomycin. The pan-European monitoring report on invasive infections showed a great variability among the countries of the European Union concerning methicillin-resistance of *Staphylococcus aureus,* between 1 and 50%. **Objectives**: in this study, we proposed proposed to achieve an analysis of microbiological data with regard to Gram-positive pathogens identified in patients with sepsis and their resistance profile. **Material and methods:** the study focused on 256 subjects diagnosed with sepsis, with positive hemocultures, admitted in the Infectious Diseases Clinical Hospital of Iasi, from November 2012 to August 2014. In order to test microorganisms' sensitivity, the Microbiology Laboratory used the diffusimetric method, each testing microcomprimate containing standard concentrations of antibiotics according to recommendations of the National Committee for Clinical Laboratory Standards. **Results:** Gram-positive germs have been identified in 56% of cases, predominantly *Staphylococcus aureus* which was present in 33% of the total number of cases. 38% of *Stafilococcus aureus* strains of were methicillin-resistant, while 34% of the coagulase-negative staphylococci were methicillin-resistant. The resistance rate of *Staphylococcus aureus* was 27% to Rifampicin, 20% to Clindamycin and fluoroquinolones and 4.5% to Biseptol. There have not been identified resistant strains to vancomycin and linezolid.

 DOI: 10.12865/CHSJ.42.03.12

Conclusions: the emerging resistance of Gram-positive bacteria isolated from both nosocomial and community infections limit the choice of antibiotherapy and is responsible for the increasing severity of disorders especially in diabetics and postoperatively. **Keywords:** sepsis, *Staphylococcus aureus*, resistance to antibiotics
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ANTIBIOTIC SENSITIVITY OF *PSEUDMONAS* STRAINS ISOLATED IN HOSPITAL " VICTOR BABES CRAIOVA"

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Objectives: retrospective study over a period of 7 years (2008 – 2014) in Hospital Victor Babes Craiova, with epidemiological aspects and antibiotic susceptibility of Pseudomonas aeruginosa, collected from various pathological products from hospitalized patients in non-ICU departments of the hospital. **Materials and methods:** were used clinical, epidemiological data of patients with Pseudomonas infections, following the evolution of annual cases, relative to age, pathological product, depending on comorbidites and organs in which the infection was isolated, following the variation of sensitivity to antibiotics of strains isolated from pathological products. **Conclusions:** 1. Total number of strains of Pseudomonas isolated, was increasing in the interval 2008 – 2014. 2. Majority location was respiratory, associated with pulmonary pathology (55%), ear(16,1 %), digestive (10,1 %),overinfected wounds (2,7%), blood cultures (1,6 %) and other sites. Were observed in children compared to adults features to determine digestive (36,8 % vs 3,3%), ear (26,3% vs 13,4 %), and respiratory (23,5% vs 62,9 %). 3. Antibiotic sensitivity was: very good for Colistin (99,1%), good for quinolones-Cefoperazone-sulbactam, Aminoglycosides: Meropenem, Aztreonam, Piperacillin – Tazobactam (82-89%); medium for Ceftriaxone and Ceftazidime (71,46% -73,8 %); ineffective-Clotrimazole, Amoxicillin –clavulanate. 4. Resistance profile to antibiotics identified the evolution of strains involved in infections predominantly community.

COMPARATIVE STUDY OF RESISTANCE TO ANTIBIOTICS OF STRAINS OF *KLEBSIELLA* ISOLATED IN URINARY AND RESPIRATORY INFECTIONS

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Background: a study of the dynamics of antibiotic resistance of *Klebsiella pneumoniae* is necessary in order to adapt therapeutic recommendations. The objectives of this paper pursue the comparative analysis of resistance to antibiotics of strains of Klebsiella pneumoniae isolated in urinary and respiratory tract infections. **Material and methods: r**etrospective study conducted between 01 January 2013 – 31 August 2014 on the resistance of *Klebsiella pneumoniae* isolated from sputum (96 strains) and urine culture (163 strains) from patients hospitalized in the "Victor Babeş" Clinical Hospital of Infectious Diseases and Pneumology, Craiova. The antibiogram was performed by classical diffusimetric method. **Results:** the resistance to antibiotics was higher in *Klebsiella pneumoniae* strains isolated from urine culture compared to those isolated in respiratory infections in case of: a) beta-lactams (ceftriaxone 45.2% versus 69.5%, cefaclor 36.7% versus 52.9%, cefuroxime 49.3% versus 61.9%, cefo-perazone-sulbactam 70.6% versus 85.7%, piperacillin-tazobactam 58.1% versus 75.5%, aztreonam 45.8% versus 66.6%, ampicillin-sulbactam 46.4% versus 69.1%, amoxi-cillin-clavulanic acid 26.8% versus 40.5%), b) quinolones (ciprofloxacin 61.8% versus 83.4%), c) co-trimoxazole (45.4% versus 82.8%). The sensitivity profile showed no major differences for: colistin (82.7% versus 81.6%), carbapenems (95.2% versus 97.8%) and aminoglycosides (72.3% versus 75.8%).
Conclusion: the sensitivity of *Klebsiella pneumoniae* to carbapenems remained high, recommending the use of these antibiotics for infections with resistant germs. The empirical use of antibiotics for urinary tract infections and invasive urologi-cal maneuvers may explain the increased resistance profile of germs isolated from urine culture.

ANTIRETROVIRAL THERAPY: SUCCESSES AND CHALLENGES?

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Introduction: along the overall history of human immunodeficiency virus (HIV) infection, antiretroviral therapy (ARVT) represents a corner-stone in the evolution of HIV pandemics. ARV drugs, classified according to the stage of viral replication they inhibit, have transformed HIV infection into a chronic illness. **Objectives**: to assess the effect of ARVT on the HIV-infected population, monitored in the Regional Centre Mures. **Material and method**: retrospective, analytical, considering the benefits of ARVT: obtaining undetectable HIV-RNA plasma viral load, reducing the vertical transmission of HIV infection, improving survival rate. **Results**: on December 31st 2014, 394 HIV-infected patients were actively monitored in the Regional Centre Mures. 329 patients benefit from ARVT, out of which 66.56% are part of the 1987-1991 cohort. The maximum survival with HIV is 23 years. Adherence to ARVT tests have proved that 56.83% patients have good and very good levels of adherence. Monitorisation of HIV-RNA plasma VL (170 tests in 2014) revealed levels < 50 copies/ml in 43.52% patients.167 patients (42.38%) are women at fertile age. 60 children were born between 2006-2014 – 57 (95%) not infected with HIV, revealing the major role of ARVT during pregnancy. **Conclusions**: the consequences of HIV infection can be controlled by sustained ARVT in patients with very good adherence. However, persistent inflammation is likely to cause future complications. **Keywords**: HIV infection, antiretroviral therapy (ART), adherence,prevention

A LONG- TERM EFFICACY OF EFAVIRENZ ANTIRETROVIRAL CONTAINING REGIMENS

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Objective: to evaluate the efficacy of long-term antiretrovirals regimens (ART) containing Efavirenz (EFV). **Material and method**: observational study which has evaluated all the patients infected with HIV (PIH) under surveillance by the Craiova Regional Center at 31 December 2014, divided in two groups: A – PIH with EFV containing regimens and B – PIH witout EFV in their current regimens. We have comparatively analysed their epidemiological, clinical, immunological and virusological data, as well as their history and adherence to ART. **Results**: from a total of 492 PIH, 115 had EFV in their current regimens (group A – 23.4%) while 377 had not (group B – 76.4%). The following data compares group A with group B: average age – 31.7±10.8 vs 28.2±8.4 years, p=.0003, average of the last CD_4 count – 620.9±408.4 vs 489.8±372.2 cells/mm^3 (p=.001), average duration of the last ART - 6.4±3.8 vs 4.4±2.8 years, p=.0001, average number of previous ART – 1.8±1.1 vs 3.4±2.1 regimens, PIH with undetectable HIV viral load on the last measurement – 61 (53%) vs 143 (37.9%), p=.004. 68 PIH from group A had an ART duration ≥ 5 years compared with 153 (40.5%) from group B. 59 PIH (51.3%) from group A were having their first ART compared with 76 PIH (20.2) from group B, p=.0001. 99 PIH (86.1%) from grop A demonstrated an adherence of ≥ 95% to ART compared with 261 PIH (69.2%) from group B. **Conclusion**: EFV containing regimens represents an efficient long-term therapeutic choice, mainly in naïve PIH with a good adherence to ART. **Keywords**: HIV, antiretroviral drugs, efficacy, Efavirenz

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THE PROFILE OF THE CRITICALLY STATE PATIENT HAVING AN INFECTIOUS DISEASE

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Background: after the cardiovascular diseases, the infectious diseases (ID) represent the second cause of mortality worldwide **. Objective:** to identify the profile of the critical patient (CPx) having an infectious diseases. **Material and**

 DOI: 10.12865/CHSJ.42.03.12

method: retrospective study (January-December 2013), based on the evaluation of 4914 patients admitted in the Infectious Diseases Department of Hospital no. 3 Craiova. CPx has been defined as a patient having organ failure and/or severe sepsis or septic shock and/or severe pneumonia (CURB65 score ≥ 4). **Results:** we have identified 163 CPx; the average age was 61 (IQR 18-95) years, with a slightly predominance of males (55.95%). We have encountered: organ failure – 65.48% of the cases, severe sepsis – 26.79%, severe pneumonia – 5.95%, septic shock – 1,78%. The following type of ID was recorded: pneumonia/pleuresy – 58.93% of cases, meningitis/encephalitis – 17.26%, digestive infections – 13.09%, urinary tract infections – 7.14%, soft tissues and tetanus – 1.2% each of them, cardiovascular infections and leptospirosis – 0.59% each of them. Etiology has been proven in 35.33% of the cases: Gram-negative bacilli – 40.68%, Gram-positive cocci – 18.64%, *Mycobacterium tuberculosis* – 13.56%, hepatitis B virus and *Toxoplasma gondii* – 6.78% each, Gram-negative cocci and Gram-positive bacilli – 3.38% each, *Cryptococcus neoformans*, *Leptospira* spp., varicella-zoster virus and influenza virus – 1.7% each. 14.88% of the CPx have had an unfavourable evolution (requiring the transfer in the intensive care units) and death has been recorded in 10.12% of the cases. **Conclusion:** the profile of the CPx is as follows; old age, having a lower respiratory tract or a neurological infection caused mainly by Gram-negative bacilli or Gram-positive cocci, developing organ failure or severe sepsis, often life threatening. **Keywords**: organ failure, sepsis, pneumonia, etiology

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BACTEREMIA WITH *SALMONELLA* SPP. - CLINICAL AND EPIDEMIOLOGICAL ASPECTS IN INFECTIOUS DISEASES HOSPITAL GALATI

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Background: clinical manifestations of *Salmonella spp.* range from subclinical to severe. Most cases are self-limiting gastroenteritis,. Fluoroquinolones and 3rd-cephalosporins are recommended for invasive infections , but therapy should take into consideration local pattern of resistance. **Objective**: comparison of characteristics of invasive infections with *Salmonella spp.* to data from "*EU Summary Report on antimicrobial resistance in zoonotic and indicator bacteria from humans, animals and food in 2013*". **Material and method:** analysis of *Salmonella spp.* bacteremia case series (8 reports) from Infectious Diseases Hospital Galati (2013-2014). **Results**: salmonella bacteremia was recorded in 8 patients, representing 16.6 % of Salmonella infections and 0.1 % of admitted cases. Patient characteristics: males (7/8) , median age 60 years [24,70] , from rural areas (5/8), association of chronic liver disease (8/8), systemic inflammatory response criteria (8/8) and digestive disorders (3/8). Evolution was favorable, with healing in all cases. Isolates were non - typhoid in Group B (2/6), C (3/6) and D (3/6) . Most infections were community acquired (7/8). All strains were susceptible to carbapenems, but some strains were resistant to Ampicillin (6/8) , Ciprofloxacin (3/5) , Tetracycline (2/8) , Furazolidone (2/8). The emergence of Ampicillin and Ciprofloxacin resistance of invasive *Salmonella spp.* isolated from patients in Galati coincides with data reported for strains isolated from meat products in the EU. **Conclusion**: invasive salmonellosis are associated with older age, male gender and chronic liver diseases. Invasive strains of *Salmonella spp.* maintain their sensitivity to 3rd-cephalosporins, remaining the first therapeutic option.

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FEATURES OF ACUTE BACTERIAL DIARRHEA IN A PAEDIATRIC UNIT

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Introduction: acute diarrheal disease (ADD) is one of the most common causes of morbidity and mortality in children. **Objectives**: epidemiological and microbiological analysis of ADD in children. **Materials and methods:** Retrospective study realised in Infectious Diseases Hospital of Craiova, between 01-01-2012,31-12-2014, on a sample of 509 patients (Px) aged 0-15 years with ADD bacterial etiology proven. **Results:** during the study, ADD represented 54.25% of all admissions, of which 506 (11.33%) with proven bacterial etiology,as follows: *Salmonella sp*. (5 Px-0.99%), *E.coli* (472 Px-93.29%), *Shigella sp.*

(29 Px-5.74%) and *Staphylococcus aureus* (3 Px-0.59%).Demographic data:report F/M=264/245; report U/R=216/293; Distribution by age belonged to 1-3 years: 221 Px (43.42%) with ADD-*E.coli* (p = 0.013). Antibiotic sensitivity for *Shigella sp* was: ceftriaxone-82.76%, colistin-89.66%, trimethoprim sulfamethoxazole- 55.18%, ciprofloxacin- 100% ampicillin- 37.94%, meropenem - 100%, ceftazidim- 79.32%, gentamicin- 100%, and for *E. coli*: ceftriaxone- 85.03%, colistin- 89.48%, trimethoprim-sulfamethoxazole -61.94%, ciprofloxacin- 93.08%, ampicillin-sulbactam-67.80%, ampicillin- 12.65%, meropenem-95.77% , gentamicin- 81.20%, piperacillin-tazobactam- 96.87%. **Conclusions**: 1. Bacterial ADD is a common cause of morbidity in pediatry, the most affected being the age group 1-3 years. 2. Bacterial ADD's etiology was represented by the *E.coli*; it was registred a high sensitivity of *E.coli, Shigella sp*. to ceftriaxone, colistin, ciprofloxacin, meropenem, gentamicin, piperacillin-tazobactam. **Keywords:** diarrheal disease, antibiotics, children

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INFECTION DUE TO *CLOSTRIDIUM DIFFICILE* – DEMOGRAPHIC, EPIDEMIOLOGICAL, CLINICAL AND EVOLUTIVE ASPECTS

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Background: infection due to *Clostridium difficile* (ICD) might be a challenge for the clinicians, having community or nosocomial origins and rising medical problems due to complications, relapses and resistance to the treatment which have an impact on medical cost and mortality. **Objective**: to analyse demographic, epidemiological, clinical and evolutive data from patients (Px) with ICD. **Material and methods**: observational retrospective study (January – December 2014) on 101 Px admitted in the Infectious Diseases Department of Hospital no. 3 Craiova. **Results**: general data: median age – 67 (IQR 16-87) years, slightly predominance of females (58,42%), median duration of admission – 8 (IQR 1-22) days. The source of the infection was not determined in 36.63% of the cases, has been considered as having nosocomial origin in 35.64% of cases or community origin in 27.72% of cases. Infection has been considered as proven in 53.46% of cases or presumable in 46.53% of cases. The ATLAS score (performed in 91 Px) has a median of 2 (IQR 0-7) points. Sepsis was diagnosed in 44.55% of Px and we have seen relapses in 14.85% of cases. Most of the Px (79.21%) have several concomitant comorbidities. Unfavourable evolutions have been noted in 9.9% of Px. **Conclusion**: ICD is frequently encountered in old Px with associated comorbidities and have often a nosocomial origin. Less than half of Px develop sepsis, relapses and deaths might be encountered. **Keywords**: *Clostridium difficile*, nosocomial, sepsis, relapses

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CLINICAL AND EPIDEMIOLOGICAL FEATURES OF SEVERE CLINICAL FORMS *CLOSTRIDIUM DIFFICILE* COLITIS IN ROMANIA – BRASOV AREA

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Objectives: to describe some epidemiological aspects and clinical course of severe *Clostridium difficile* colitis in patients admitted in the Infectious Diseases Hospital of Brasov - Romania. **Material and methods:** a retrospective study on 22 patients hospitalized in the period November 2012-April 2014 with severe forms of proven diagnosis of *Clostridium difficile* colitis. We analyzed age and sex of patients, previous hospitalizations, associated chronic diseases, type of diarrheal stool, frequency of flatulence, some laboratory disturbances, evolution with proper treatment.**Results**: severe forms accounted for 20,75 % of all cases of *Clostridium difficile* colitis; 68% of cases were found in patients aged over 70 years; 90,91 % of patients had previous recent hospitalizations and in the same proportion chronic diseases associated (particularly cardiovascular diseases – 63,64 % cases), 45.45% with 3 or more comorbidities. From the point of view of clinical signs all patients had watery diarrhea (type 7 on Bristol stool scale), associated with mucus in 31.82% cases and flatulence in 81.82% of patients. We found anemia in 77.28% of cases, leukocytosis over 20,000 / mm3 in 45.45% of patients and

 DOI: 10.12865/CHSJ.42.03.12

hypoproteinemia in all investigated cases. Evolution was favorable in 77.28% of cases. **Conclusions**: severe forms of *Clostridium difficile* colitis are not rare. Frequency of severe forms is higher in elderly patients with multiple comorbidities and recent hospitalizations. Flatulence is common in the clinical picture of severe forms, in addition to watery diarrhea stools. The treatment of severe forms is complex, focused on the one hand on the basic disease and imbalances caused by this and on the other hand on the associated diseases. **Key words:** *Clostridium difficile*, severe forms
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TIGECYCLINE IN ANTIMICROBIAL TREATMENT IN AN INFECTIOUS DISEASES HOSPITAL

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ERADICATING HELICOBACTER PYLORI INFECTION – FROM GUIDELINES TO CLINICAL PRACTICE

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DIGESTIVE INFECTIONS DUE TO *CLOSTRIDIUM DIFFICILE* (CDAD), FROM THE DIAGNOSIS TO THE TREATMENT

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Infections due to Clostridium difficile (CDAD) have become a major public health problem. Their recognition, diagnosis and treatment is essential. Coprocultures are not clinically relevant in the absence of toxin detection. Epidemiological context is considered as sufficient to suspect the diagnosis. Around 10% of cases are of community origin. **Objective:** to evaluate incidence of CDAD and the cost of diagnosis. **Material and method:** a rapid test for diagnosis of CDAD has been used in 106 cases. Test has been considered positive when both the Clostridium difficile antigen and toxins were positive. **Results:** the test has been found positive in 32 cases (30%); other 32 cases (30%) shows positivity only for the Clostridium difficile antigen. The test was negative for the rest of the cases. The estimated cost for a positive test was 150 RON. **Conclusion:** 1. Incidence of CDAD is a major public health problem. 2. Rapid diagnosis is necessary or sufficient for starting the treatment? 3. Is CDAD a form of resistance to antibiotics which requires a review of the antibiotics usage for treatment and / or prophylaxis of the infections?

RISK FACTORS ASSOCIATED WITH *HELICOBACTER PYLORI* INFECTION IN HIV-POSITIVE PATIENTS MONITORED IN THE CLINIC OF INFECTIOUS DISEASES TÎRGU MUREŞ

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Introduction: digestive tract symptoms represent one the most frequent complaints of patients infected with human immunodeficiency virus (HIV). Hence - the utility of studying *Helicobacter pylori* infection among HIV-positive individuals, since this bacteria is a common cause of gastritis / peptic ulcer in the general population. **Objective**: studying risk factors associated with the presence of *Helicobacter pylori* among HIV-infected persons. **Material and method**: retrospective, analytical, case-control study, on two groups of HIV-positive patients monitored in the Clinic of Infectious Diseases Tîrgu-Mureş: group A – 37 *Helicobacter pylori*-positive patients, group B – 54 *Helicobacter pylori*-negative individuals. We investigated various risk factors associated with the presence of *Helicobacter pylori* in HIV-infected persons. **Results**: we obtained positive, but not statistically significant associations between the presence of *Helicobacter pylori* and low educational level (p=0.3703, OR=4.167), the absence of stabile occupation (p=0.4713, OR=1.648) and negative, but not statistically significant association between digestive tract infections with *Helicobacter pylori* and fungi (p=0.5150, OR=0.5074). Patients co-infected with *Helicobacter pylori* had higher levels of CD4+ T-cells (median = 356 cells/µL) than *Helicobacter pylori*-negative ones (median =

265 cells/μL), corresponding to a positive statistically significant association between *Helicobacter pylori* and antiretroviral therapy (p=0.0322, OR=2.700). **Conclusions**: *Helicobacter pylori*-HIV co-infection associates both common risk factors to those registered in the general population and specific risk factors, characteristic for HIV-immunocompromised subjects. **Keywords**: *Helicobacter pylori*, human immunodeficiency virus, digestive tract
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ETIOLOGICAL, CLINICAL AND BIOLOGICAL CONSIDERATIONS IN URINARY TRACT INFECTION IN CHILDREN

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Introduction: the urinary tract infection (UTI) in children is considered the 3rd most frequent cause of illness (after respiratory and digestive infections). **Objectives:** to study some epidemiologic, clinical and biological aspects in children with UTI, admitted to a pediatric clinic. **Material and method:** we performed a retrospective study regarding UTI in children aged 0-16 years, admitted to the 2nd Pediatric Clinic, Emergency County Hospital in Craiova, from 2009 to 2013. The study group consisted of 224 children with UTI (61 infants, 28 children aged 1-3 years, 48 children aged 3-6 years, and 87 children over 6 years). **Results:** UTI prevalence was 2.5%. Clinical manifestations present in infants and toddlers - fever (75%), restlessness (40%), alimentary vomiting (34%), food refusal (28%), and convulsions (2%), while in schoolers - abdominal pains (59%), dysuria (38%), and pollakiuria (24%). Bacterial etiological spectrum: *E. coli* 75 cases, *Klebsiella* 14, *Proteus* 7, *Enterobacter* 4, mixed infections *Klebsiella /Enterobacter* 4, *Klebsiella /E. coli* 5, *E. coli/Proteus* 3 cases; in 43 cases, the urocultures were negative, and the UTI diagnosis was based on clinical and laboratory criteria. **Conclusions:** UTI prevailed in newborn and toddler boys and schooler girls. E. Coli was the most frequent etiological agent. Factors favouring UTI: anomalies of the reno-urinary system (vesicoureteral reflux), renal lithiasis, stasis at the level of the digestive system (constipation, intestinal parasitoses) and malnutrition. Antibiotic sensitivity of the microbial stems isolated in children with UTI was for Ceftibuten and Sulperazone in *E. coli*, Sulperazone and Imipenem in *Klebsiella*, Imipenem and Linezolid in *Proteus*. **Keywords**: urinary tract infection, children
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ETIOLOGIC SPECTRUM OF SPONTANEOUS BACTERIAL PERITONITIS STUDY IN A GROUP OF PATIENTS SUFFERING FROM LIVER CIRRHOSIS

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Background: spontaneous bacterial peritonitis (PBS) represents the most common infectious complication in cirrhotic patients. **Objective:** the study of the bacterial spectrum causing PBS in a group of patients with hepatic cirrhosis. **Material and method:** the study was performed on a group of 64 patients, average age 46 years, suffering from hepatic cirrhosis with one episode of PBS, who were admitted to the Emergency County Hospital Craiova, on the II-nd Medical-Clinic, within a period of 12 months. The diagnostic of cirrhosis was established using clinical, biological and imagistic criteria, and the diagnostic of PBS was established using cytological and bacteriological analysis of the ascites fluid. Patients suffering from hepatocellular-carcinoma and portal-vein thrombosis were excluded from the study. All patients included in the study were evaluated by anamnesis, clinical examination, hematological, biological (GOT, GPT, bilirubin, blood concentration of albumin, prothrombin-time, antigen-HBs, antibodies anti-HCV) and imagistic characteristics. The white blood cells count, leukocyte formula, glucose level, albumin and LDH, as well as cultures, Gram and Ziehl-Nielsen colorations were evaluated from the ascites. **Results:** within the study group the most frequent pathogens were the Gram negative germs such as *Escherichia coli* and *Klebsiella* spp, responsible for more than half of the infections. The Gram positive germs most frequently involved (22%) were *Streptococcus pneumonie* and *Streptococcus viridans*. About 7% of the infections were caused by

 DOI: 10.12865/CHSJ.42.03.12

Enterococcus spp. **Conclusions:** the most common etiology is represented by the Gram negative germs. Knowing the etiologic spectrum influences the choice of antibiotic therapy until getting the bacteriological result. **Keyword*:*** cirrhosis, peritonitis, etiology
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CLINICAL AND EPIDEMIOLOGICAL ASPECTS OF INFLUENZA AND SERIOUS RESPIRATORY INFECTIONS DURING 2014-2015 SEASON IN CONSTANTA

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Introduction: influenza and severe acute respiratory infections are an important public health issue due to the unpredictability in what concerns the circulation of the influenza viral types and because of the receptive human mass characteristics. **Objectives**: assessing the circulation of the viral types during the 2014-2015 flu season in Constanta and defining the particularities of the influenza that lead to the hospitalization of the patients in the CHID Constanta. **Resources and methods**: the retrospective analysis of the influenza cases confirmed in the laboratory by PCR. The analysis was based on the following factors: influenza strain, characteristics of the hospitalized population, immunization status and the clinical forms of the disease. **Results**: out of 358 patients hospitalized and confirmed with influenza, 55 have developed serious acute respiratory infections. The main circulating influenza strain was type B (76.8%), followed by the subtypes A H3 (15.64%) and A H1N1 (7.26%). There has been also a co-infected case with two strains. **Conclusions**: the main influenza type B in a receptive population determined an increased demand of medical care. However, the SARI cases remained at a relatively low level during the 2014-2015 season and there was no death occurrence due to influenza in Constanta. **Keywords**: influenza, viral types, immunization, severe acute respiratory infection.

CLINICAL ASPECTS, DIAGNOSIS, TREATMENT, EVOLUTION OF INFLUENZA CASES IN 2014/2015 SEASON IN COUNTY MURES

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Introduction: seasonal flu is a contagious disease which has extremely high epidemic more frequently in winter. In the last years in Romania the number of confirmed cases increased, more likely due to virological surveillance and diagnosis. **Objectives**: clinical monitoring, biological and evolutionary patients with severe clinical forms of flu Mures County. **Material and methods**: the study was conducted on a group of 17 patients with confirmed influenza virus infection in January-March 2015, which were hospitalized and monitored in Clinic of Infectious Diseases and Intensive Care Unit II. Serological determinations were performed at the National Institute Ioan Cantacuzino Bucharest by nasopharyngeal Polymerase Chain Reaction Real Time method (RT-PCR). In the study were supervised secondary diseases and complications associated with influenza infection. **Results**: patient age ranged between 1-60 years, female sex predominated. Virus subtypes identified were A (H1) pdm09 - 8 patients, A (H3) -7 patients; influenza virus B-2 patients. From all patients confirmed, four cases had imposed a monitoring Intensive Care Unit, and 3 patients were intubated and mechanically oro-tracheal ventilated. The clinical forms of the disease were probably due to more severe risk factors (cardiovascular disease, diabetes, neuroimmunological diseases, pregnancy). Patients received antiviral treatment with Oseltamivir and antibiotic. **Conclusions**: associated disorders with patients studied were important risk factors in the development of respiratory complications. **Keywords:** flu, diagnosis, treatment.
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PREGNANCY AND THE INFECTION WITH INFLUENZA IN THE 2014 – 2015 SEASON

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Objective: the analysis of the severity of the infection with influenza viruses and of their complications at pregnant women. **Material and method**: retrospective study on three patients hospitalised in the January – March 2015 period at the Infectious Diseases Clinic 1 Tg-Mures with the diagnosis of influenza and pregnancy in evolution. The positive diagnosis of influenza was established based on the RT¬-PCR real time test of the naso-pharyngeal exudates on the day of coming to the hospital and at less than 7 days from the start of the disease. **Results**: the patients were aged 19 – 29 and their pregnancy was between 7 and 20 weeks. Two patients were confirmed with infection with AH3 influenza virus and one patient with the B influenza virus. At hospitalisation, none of the patients presented signs of acute respiratory insufficiency. The most frequent complications were trachea – bronchitis in 3 cases and secretory otitis media at one patient. All three patients received antiviral treatment with Oseltamivir for 7 days. None of the patients had been vaccinated against influenza. **Conclusions**: the infection with the AH3 and B influenza viruses is not associated with severe evolution. **Keywords**: pregnancy, AH3 influenza virus, B influenza virus
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CAUSES OF MORBIDITY AND MORTALITY AMONG HIV INFECTED PATIENTS WITH ANTIRETROVIRAL TREATMENT

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Objective: to identify the main causes of morbidity and mortality in HIV infected patients (PIH) treated with antiretrovirals (ARV). **Material and methods**: retrospective study (January – December 2013); we have evaluated 212 PIH from Dolj county, treated with ARV, under surveillance of Craiova Regional Center. We have analysed the causes that required hospital admission and/or lead to the death of PIH. **Results**: 92 PIH (43.4%) required hospital admission and 4 death (1.9%) has been noted. Characteristics of hospitalized PIH follows: gender distribution male / female = 42/50 (45.6% / 54.4%), average age = 28 ± 9.2 years, clinical and/or immunological AIDS status – 77 PIH (83.7%), average duration of ARV treatment = 11.6±4.8 years, average number of ARV regimens = 4.6±2.3, median CD_4 count=308.5 cells/mm^3. The main causes of morbidity: non-tuberculous respiratori infections – 32 PIH (34.8%), reno-genital sufferences – 12 PIH (13.1%), digestive ailments – 11 PIH (11.9%), tuberculosis – 10 PIH (10.9%), neurological and mental sufferences – 6 PIH (6.5%). Average time of hospital admission = 15.1 days, average hospital admission/PIH = 1.8/year. 38 PIH have had ≥2 admissions. Causes of death: TB – 3 PIH, lung cancer – 1 PIH. **Conclusions**: the main causes of morbidity and mortality in PIH treated with ARV was respiratori infections and reno-genital sufferences; TB is an important cause of morbidity and mortality in PIH. **Keywords**: morbidity, mortality, HIV, antiretrovirals
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CHANGES IN LIVER FIBROSIS IN PATIENTS WITH VIRAL CHRONIC HEPATITIS C – CORRELATION WITH THERAPY RESPONSE

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Introduction: non-invasive methods for assessment of liver fibrosis (FibroScan) are used in patients with chronic hepatitis C (HCV). **Objectives:** evaluating the effect of double therapy with Pegylated Interferon (PegINF) and Ribavirin (RBV) on liver fibrosis in treated chronic HCV patients and the relation between IL-28B polymorphism, sustained virological response (SVR) and the decrease of liver stiffness. **Methods:** in 102 chronic HCV patients treated with PegINF and RBV liver fibrosis was

 DOI: 10.12865/CHSJ.42.03.12

assessed by FibroScan before and after therapy. The IL-28B SNP rs 12979860 was analysed by genetic tests. **Results:** in responders the ratio of patients with F3/F4 fibrosis decreased from 14.81% to 7.41%, and of F1/F3 patients from 47.04% to 33,33%. The percent of F0 patients increased from 48.15% to 59.26%. In non-responders F3/F4 patients percentage increased from 38.10% to 52.38%, that of F1/F3 patients increased from 47.62% to 33.33% and F0 patients percentage remained constant at 14.29%. In multivariate analysis responder status was associated with decrease of fibrosis score of 1,24 grades (p=0,025) and the decrease is 1,32 grades higher for TT allele (p=0,014), and CC allele of Il-28B SNP was associated with SVR (OR=31,66, p=0,003). **Conclusion:** our study showed a significant reduction of liver fibrosis in all patients after the treatment, even higher in patients with IL-28B TT genotype.

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CIRRHOSIS – A RETROSPECTIVE STUDY FOR 24 MONTHS

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Introduction: cirrhosis represents the final stage of chronic hepatic disease, it is irreversible, and treatment usually focuses on preventing progression and complications. **Objective**: we evaluated the specific aspects of chronic hepatic disease in the patients admitted in the Infectious Diseases Hospital Iasi from January 2013 – December 2014. **Material and methods**: our retrospective study included 109 cases of cirrhosis of viral or toxic etiology, in the 24 months period. **Results**: in the 109 cases sample, 46.78% were female, 53,21% male; 46.78% from an urban area and 53,21% rural; more frequently in the 41-70 year age group; 36.69% were diagnosed with decompensated parenchymal cirrhosis, 8.25% had decompensated vascular cirrhosis, 35.77% had decompensated mixed cirrhosis and 19.26% had compensated liver cirrhosis. Etiology: 43% cases virus C, 8% virus B, 5% virus B + D, and 29% have toxic ethanolic etiology. Diagnosis: 12% as a result of the superior digestive endoscopy with esophageal varices, 36% of them associating a history of upper digestive hemorrhagy. Ascites has been observed through abdominal ultrasound examination at 7% of cases. The appearance of the liver to abdominal ultrasound examination revealed an enlarged, nodular liver in 38% of cases and 14% of the patients had a significantly smaller liver. **Conclusion**: our study revealed that the disorder is more common in patients aged over 40 years, both in terms of women and men. The etiology of liver cirrhosis is viral B, C or B+D, with complications for less than half of the patients included in the study. **Keywords**: cirrhosis, viral/toxic etiology

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EVALUATING THE ROLE OF SERUM BIOMARKERS IN PREDICTING MORTALITY IN SEPSIS AND BACTEREMIA PATIENTS

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Introduction: sepsis constitutes the principal cause of mortality in critical patients. Validating new serum sepsis biomarkers ***(BM)*** contributes not only to improving diagnostic performance, but also improves the capacity to evaluate the prognostic. **Objective**: evaluating the mortality prediction capacity in sepsis patients with bacteremia of new BM: suPAR (soluble urokinase-type plasminogen activator receptor), ANG-2 (angiopoietin-2) and TIE2 (tyrosine-kinase receptor). **Materials and method**: we selected 49 patients with at least 2 SIRS criteria and with clinical signs of an infectious process. They had determined on the day of admission, serum levels of suPAR, ANG-2 and TIE2 through the ELISA method and 3 sets of hemocultures were drawn. The patients were divided into 2 groups: group A, bacteremia patients (n=14) and group B, patients without bacteremia (n=35). Mortality prediction was done using the ROC curves for the plasma level of the studied BM. **Results**: the registered mortality was 85,7% in group A and 74,3% in group B (p>0.05). Out of the studied biomarkers, suPAR registered the largest difference between the groups (14,29 ng/ml vs 9,85 ng/mL, p=0.008). In bacteremia patients, the optimal cut-off values of suPAR, ANG-2 and TIE2 in predicting mortality was 11,5

ng/mL, 6,705 ng/mL and 4,08 ng/mL, AUC for the last one being superior (0,75 vs 0,66 for the first two BM). **Conclusions**: serum biomarkers levels are significantly influenced by the presence of bacteremia and increased values correlate with sepsis prognosis. **Keywords**: biomarkers, sepsis, prediction

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THE MORBIDITY EVOLUTION OF VACCINE – PREVENTABLE DISEASES IN DOLJ COUNTY

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The control of vaccine-preventable diseases (VPD) requires ensuring proper immunization programs in order to achieve a minimum 95% vaccination with a nationwide coverage. **The objectives** of the study follow the immunization program‘s results by analyzing the morbidity evolution of VPD in the Dolj county. **Material and** m**ethods**: the VPD morbidity (number of disease cases reported annually per 100,000 persons) was analyzed based on the Department of Statistics and Computer County Public Health Directorate in the range 1994-2013. **Results**: measles recorded a lower average morbidity (1.62 $^{0}/_{0000}$) with epidemic increases in 1997-1998 (120 $^{0}/_{0000}$) and 2012 (192 $^{0}/_{0000}$). Rubella presented multi-variations (between 0.27 and 124 $^{0}/_{0000}$) reaching a maximum in 2012 (192 $^{0}/_{0000}$). Mumps infection had a marked decrease in local morbidity since 2006 after the introduction of vaccination (from 161.1 $^{0}/_{0000}$ to 1.31 $^{0}/_{0000}$). In local pertussis, the morbidity continuously decreased (from 3.95 $^{0}/_{0000}$) and there were no reported cases since 2006. Diphtheria - no confirmed cases. Tetanus had a local average morbidity of 0.14 $^{0}/_{0000}$ with growth in 2011 (0.82 $^{0}/_{0000}$). Suspected cases of polio recorded only oral vaccination associated between 1996-1997 when morbidity was 0.7 $^{0}/_{0000}$. In acute viral hepatitis type B, morbidity decreased from 36.8 $^{0}/_{0000}$ (1995) to 3 $^{0}/_{0000}$(2013). **Conclusions**: the application of immunization programs has led to effective control of BPV (polio, diphtheria) and has significantly reduced morbidity mumps, whooping cough, acute viral hepatitis type B. Sub-optimal vaccine coverage leads to increased susceptibility and transmission risks of restoring infectious agents in the receptive population. **Keywords**: vaccine-preventable diseases, morbidity, Dolj

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FEATURES OF INFECTIONS IN CHILDREN SUFFERING FROM MALNUTRITION

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Background: the World Health Organization estimates that malnutrition is responsible of 54 percent of child mortality worldwide (incriminated for about 1 million deaths per year in paediatric patients). Infectious diseases are often diagnosed in paediatric population, especially in cachectic patients, when could evolve towards sepsis. Sepsis is defined as an systemic inflammatory response syndrome (SIRS) caused by an infection. **Material and method:** authors conducted a prospective-retrospective study about cachectic patients, using their clinical worksheets. The length of the studied period was from january 2013 to december 2014, during the admission of these patients in First Pediatrics Clinic (Emergency Hospital of Craiova. Authors diagnosed cachexy in children whose BMI was below 5th percentile and below 3rd standard deviation. **Results**: of a total of 5438 patients who were admitted in the last two years, in First Paediatrics Clinic, 1,5% (82 patients) were cachectic. We found that within the deceased children (in 2013-2014), the incidence of cachexy was 25%. In our study, poor state of nutrition was related to: incorrect feeding or improper care, frequent infections and congenital defects or a combination of the previous causes. Congenital defects found were: 21-trisomy, heart malformations, Seckel syndrome, microcephalus, hydrocephalus. **Conclusions**: in thin children, with birth malformations, pneumonia was the main cause of admission. Infections produced malnutrition and cachexy promoted severe sepsis that led to death of 10% of septic patients. Cachexy, especially associated with congenital defects, remains an important cause of immunodeficiency which promotes severe, even lethal infections.**Keywords**: cachexy, children, infection, sepsis.

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 DOI: 10.12865/CHSJ.42.03.12

ROTAVIRUS DIARRHEA IN CHILDREN – EPIDEMIOLOGIC AND CLINICAL ASPECTS

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Introduction: Rotavirus represents the most frequent cause of infectious diarrhea in infants and toddlers. **Objective:** epidemiologic evaluation of the clinical manifestations and of the evolution of the Rotavirus diarrhea in children. **Material and method**: children with Rotavirus diarrhea admitted to the 2nd Pediatric Clinic of the Emergency County Hospital in Craiova, from 1.01.2012 to 31.12.2014. **Results:** in this period of time, 55 children with Rotavirus diarrhea were admitted: 19 (34.5%) infants, 26 (47.3%) children 1-3 years and 10 (18.2%) children 3-6 years. *Sex ratio (M/F)*: infants 11/8, 1-3 years 14/12, 3-6 years 5/4; according to rural and urban regions (U/R): infants 12/7, 1-3 years 20/6, 3-6 years 8/2. *Clinical manifestations:* watery stools 55, vomiting 38, fever 25, inapetence 20; the acute dehydration syndrome was present in 42 (76.4%) children. According to season: 21(38.2%) children were admitted in winter, 16 (29.1%) in spring, 7 (12.7%) in summer and 11 (20%) in autumn. Carential diseases: anemia in 26, rickets in 28, protein-calorie malnutrition in 14. The average period of hospitalization 7.19±1.97 (3-13) days. The evolution was favorable in all cases. **Conclusions.** 1. Rotavirus diarrhea was more frequent in children aged 1-3 years, in male children and in children coming from urban areas. 2. The acute dehydration syndrome was present in more than 2/3 of the cases. 3. Most cases were admitted in winter and spring.

Keywords: diarrhea, Rotavirus, children

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POSTSURGERY MENINGITIS WITH *KLEBSIELLA PNEUMONIAE* – CASE REPORT

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UNDIAGNOSED RASH SYNDROME IN A SMALL CHILD WITH AH1PMD09 FLU WITH FATAL OUTCOME

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Introduction: the incidence of rash (maculopapular) associated with influenza (I) is about 2%. It usually occurs in children. In Romania there have been two cases of I with rash (measles like). Patient 13 months old, with mother confirmed with I type A H3, was admitted to the Infectious Diseases Clinic I, Tg.Mureş for acute gastroenteritis. After 48 hours she vomits incoercibly, with a bulging fontanelle. Eye bottom examination shows perivascular hemorrhage. Transfontanellar ultrasound raises suspicion of cerebral haemorrhage, she was admitted to Pediatric Clinic. Cranial CT examination infirm diagnosis (revealed otomastoiditis, maxillo-ethmoid sinusitis). Nasopharyngeal swab (RT-PCR) positive for influenza type A H1pdm09. Result. It establishes the diagnosis of pandemic influenza A H1 complicated with otomastoiditis, maxillo-ethmoid sinusitis. During antibacterial therapy she develops: fever , macular erythematos rash on the face, trunk, with a tendency to confluence, cough, vomiting, diarrhea. The retransfer in our clinic with suspected rubella takes place. Serological examinations refute the diagnosis. We suspected a gram-positive sepsis (procalcitonin> 10ng/ml). Recieved antibiotics (Meropenem, Vancomycin), anti-inflammatory, depletion. Unfavorable evolution: worsening general condition, hemorrhagic lesions, renal, liver impairment, leading a transfer to Intensive Care Children Clinic where death occurs after 5 days support of vital functions. **Conclusions**: influenza, in a small child unvaccinated, but without other predisposing factors, was fatal. The difference in type of influenza viruses isolated from the mother and child, raise the suspicion of a mixed viral infection with subsequent superinfection in hospital conditions. The rash raised differential diagnostic problems.

Keywords: influenza A H1pmd09, rash, death

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PARTICULARITIES OF SEPSIS IN NEWBORN. CLINICAL - CASE PRESENTASION

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Neo-natal sepsis may be early (installed in the first 7 days of life) or late, presenting after the first postnatal week. The early is produced by infection transmitted from the mother and the late sepsis-caused by various community or nosocomial bacteria (most commonly incriminated: *Streptococcus* gr. B, *E. coli*). Clinical case described is a newborn-A.U. 7 days old, admitted to the Pediatric Clinic of Craiova, critical care compartment, on 13/02/2015. Reasons for admission: fever (38.5 to 39 ° C) and vomiting food and faeces subsequently bilious, accompanied by flatulence and fetid diarrhea. From medical history remember that it was a underweight newborn by young, healthy genitors, still having a preschool child without chronic illness. On examination at admission were recorded: G = 2700g (2550 at discharge), clinical signs of dehydration, skin and mucous jaundice, tachypnea 78 breaths / min, tachycardia, 160-190 b / min, archaic reflexes present). Complementary examinations revealed: initial leukopenia, leukocytosis later - over 19500 / mmc, markers of inflammation present, and the stool, nasal and throat swab was detected *E. coli*. Followed etiological treatment with Meronem, symptomatic and pathogenic, the three-day dietary total parenteral nutrition, followed by refilling delactosed milk powder. Because gastric tube was removed f aeces content three days and new-born presented ileus, exploratory laparotomy was performed, but wasn not intestinal obstruction. In conclusion, it was a digestive severe sepsis with ileus, imitating acute surgical abdomen, but the infant was cured by medical treatment. **Keywords:** newborn, sepsis.

SEPSIS WITH MULTIPLE ETIOLOGY ASSOCIATED TO RITUXIMAB THERAPY FOR B-CELL NON-HODGKIN LYMPHOMA - CASE REPORT

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Introduction: Rituximab is a monoclonal antibody targeting CD20 B-cell used in Non-Hodgkin lymphoma (NHL), chronic lymphocytic leukemia and some autoimmune diseases' treatment. This molecule caries a high risk of secondary infections, particularly after long term immunosuppression. **Case-report**: the patient was admitted for one day onset of fever and chills, 2 weeks after the rituximab infusion. Her recent history revealed an abdominal sepsis with *E. coli* (6 months earlier) and recurrent urinary tract infections. Clinical findings at admission: fever and important asthenia. Lab findings: thrombocytopenia, normal neutrophils count, positive C reactive protein and 2 consecutive positive blood cultures (24 hours interval) – first for *E. coli* and the second for *Streptococcus mitis*; also a positive serum galactomannan antigen (GMAg). The first choice antibiotic was Meropenem, de-escalated to Ceftriaxone+Gentamicin after the blood-cultures results. She received also a short course of antifungal therapy (an echinocandin), the invasive aspergillar disease being ruled out by repeated negative GMAg and normal thoracic scan. The echocardiography ruled out endocarditis, the abdominal imagery and uroculture ruled out roughly an abdominal infectious focus. The total antibiotic course was 2 weeks, with full recovery. **Conclusion**: plurietiologic sepsis can be expected in immunocompromised host. Some etiologies can be ruled out after careful complementary exams (Aspergillus in this case). Without clear exclusion exams, the treatment must cover all founded etiologies. **Keywords**: rituximab, sepsis, plurietiology

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DIFFICULTIES OF NERVOUS SYPHILIS DIAGNOSIS IN A PATIENT WITH MENINGOENCEPHALITIS

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Introduction: Syphilitic meningoencephalitis could be a clinical presentation of the tertiary syphilis, developed after a variable length of time after the primary infection. The prevalence of nervous syphilis is low in Europe, but 1/3 patients with untreated primary syphilis should develop thorough tertiary clinical stage. A 59 old man from rural living area, chronic alcohol user, smoker, was diagnosed with neuropsychiatric syndrome, based on clinical criteria, cytological and biochemical features and positive Ac-IgM anti-Treponema pallidum

 DOI: 10.12865/CHSJ.42.03.12

in cerebrospinal fluid. The suspicion of nervous syphilis was less considered because of the alcoholic neurocognitive deterioration, without data of the primary infection. A subclavian lung radiologic lesion and concomitant tuberculosis criteria of probability (according Marais score) required the consideration of this diagnostic and specific combination therapy. **Conclusions:** Although the tertiary syphilis is a rare etiology, Treponema pallidum should be investigated in patient on adult age for the diagnosis of the meningitis with clear cerebrospinal fluid. **Keywords**: nervous syphilis, meningoencephalitis, tuberculosis
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ABDOMINAL ACTINOMYCOSIS IN AN IMMUNECOMPETENT HOST – CASE REPORT

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Introduction: abdominal actinomycosis is a rare chronic granulomatous disease that usually affects the appendix and ileo-cecal region. Frequently is developed after surgery, trauma, neoplasia, perforated viscus or is associated with intrauterine contraceptive devices' use. **Case-report**: the patient (24 years old) was admitted in a surgical unit in January 2015 for: fever, nausea, vomiting and intense abdominal pain. Clinical exam revealed an appendicular mass and she underwent appendectomy and partial cec-ectomy with excision of a voluminous cvasi-capsulated appendicular tumor, with macroscopic pus areas at dissection. Was firstly interpreted as malignancy. The histological examination found extensive ulceration of the mucosal epithelium, acute inflammatory granulation tissue in the lamina propria, abscessed in patches with extension to the others parietal layers, which includes *Actinomyces* colonies, and a surrounding dense parietal fibrosis, concluding: appendicular actinomycosis with periappendicitis. She was addressed to our clinic for further evaluation. Anamnesis: no predisposing factors. Clinical exam: supple post-surgery scar, no abdominal pain and discrete painless enlargement of inguinal lymph nodes. Lab: negative inflammatory tests; no immune-deficit. The reexamination of histological pieces confirmed the diagnosis. The abdominal-pelvic MRI: thickness of ileum with gadolinium enhancement. She received iv Penicillin 12MU/day, 14 days, to be continued with orally long-term Amoxicillinum. Next evaluation was scheduled after 3 months. **Conclusion**: it is a particular case of a very rare disease appearing in an immunocompetent young patient, without predisposing factors. The diagnosis was done by pathologist, after excision of a "voluminous appendicular tumor". **Keywords:** appendicitis, actinomycosis, immunocompetent host
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HELICOBACTER PYLORI IN THE FAMILY THE TREATMENT OF FAMILY MEMBERS INFECTED WITH HELICOBACTER PYLORI. CLINICALLY ASYMPTOMATIC. RESEARCH ON 151 FAMILIES WITH 388 MEMBERS, IN THE PERIOD 2005-2008, IN PRAHOVA COUNTY

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In internal medicine, *Helicobacter pylori* bacillus introduced the concept of infectious disease in the etiopathogenetic "*continuum"*: acute, chronic, atrophic gastritis, enteric metaplasia, gastric and duodenal ulcer, gastric cancer, Malt lymphoma; consequently, the WHO 1995 categorised it as group I carcinogenic agent for gastric cancer. Gastric cancer represents 8% of cancers total number and 10% of the annual quantum of cancer deaths, and also a decrease in new cases, resulted from the decrease of the *H. pylori* chronic infection. In Romania, gastric cancer is the second after the colon cancer. **Purpose**: finding the "native" *H. pylori* carriers in order to apply the primary preventive etiotropic treatment in the epidemiological principle: every H. pylori carrier must be treated. These "natives" are family members out of whom one presents the clinical symptomatology specific to the *H. pylori* infection, who was adequately

treated with medicines (the family's "signal" sufferer). By ascertaining the intra-family *H. pylori* transmission in a female patient with repeated severe forms of toxicosis at *Helicobacter pylori*, we found *H. pylori* in the patient's mother and husband, clinically asymptomatic; we applied the same therapy to them also, with prompt and lasting effects on the clinical state of the female patient, thus proving the role of the intra-family source in *H. pylori* transmission, which sustains the toxicosis state of the patient. **Methodology**: we researched the presence of the anti-H. pylori IgG antibodies through recognised qualitative serological tests (2) in 151 families with 388 members from rural and urban environments, aged between 10 months and 85 years; detected present in 291/75%, 142 F and 149 M and absent in 97/25% members 54 F and 43 M, plus 140 unknown asymptomatic *H. pylori* carriers. We used the following treatment plan: day I-VII: IPP 2x20 mg/day ; De-NOL: 120 mg x4/day, Klacid: 25 mg x4/day, DUOMOX: 1000 mg x 2/day, and in the days VIII-XXVIII: OMEZ: 20 mg/day and De-NOL: 120 mg x 2/day, recommendation according to Maastricht, as well as our own experience and confidence. The prolongation of the IPP and De-NOL treatment was done in order to ensure the deactivation of *H. pylori* in areas less accessible to antibiotics. Adverse reactions: two female patients had nausea, bilious vomiting, and a 56 years old female sufferer had micropapular eruptions on the lower limbs. **Conclusions**: we applied the primary etiotropic prophylaxis treatment in the etiopathogenetic "continuum" of the *H. pylori* infection in the family as a basic epidemiological principle of decontamination of the primary infection focus. We have no knowledge of any similar research. Through the acknowledged accord of all the native *H. pylori* carriers we also included the Maastricht III recommendation to follow the medicine treatment on "patient's request". The use of quadruple therapy and particularly of Clarithromycin (KLACID) comprised medicines that, through their own action, but also in conjunction, blocked all the "evil" ways of action of *H. pylori*. The application of this therapeutic methodology of primary etiotropic epidemiological prophylaxis is validated "in integrum" by the conclusions and recommendations Maastricht IV 2010 Florence in the preventive role of the decontamination of the individual immunopathological focus, as well as of the "family infection focus ", with a role in gastric cancer prevention . **Key words**: *Helicobacter pylori*, family, clarithromycin, family infection focus

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ARFI (ACOUSTIC RADIATION FORCE IMPULSE) – COMPARISON BETWEEN INACTIVE HBV INFECTION AND OTHER HEPATIC DISEASES

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NONINFECTIOUS CHRONIC MENINGITIS: CASE REPORT AND LITERATURE REVIEW

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Introduction: chronic meningitis (CM), defined as meningitis lasting for four weeks, is a complex entity with both infectious and noninfectious causes. Patients with CM usually have a sub-acute onset of symptoms including fever, headache and vomiting. **Objective:** to draw attention to noninfectious etiologies of CM. **Material and methods**: case report of 37 year-old white male hospitalized for recurrent headache lasting for eight weeks. We reviewed the literature regarding non-infectious causes of CM. **Results:** the clinical exam was normal. MRI showed diffuse meningitis. The first lumbar puncture showed: 35 cells/mm^3 with CSF proteins of 158 mg/dl and CSF glucose of 53 mg/dl (plasma glucose 109 mg/dl) and normal CSF lactic acid. CSF PLEX-ID test identifying bacteria and fungi was negative. Blood tests were normal except for C reactive protein (4.54 mg/dl). The serologies for HIV, syphilis, *B.burgdorferi* were negative. Chest X-ray was normal. We initiated standard anti-tuberculous treatment, although the CSF was not suggestive for tuberculosis and the PCR for *M.tuberculosis* was negative, but the symptoms and CSF remained unchanged, therefore the anti-TB treatment was stopped. Angiotensin converting enzyme and the antibodies for lupus

 DOI: 10.12865/CHSJ.42.03.12

were negative (anti-dsDNA, ANA, anti-SS-A, anti-SS-B). Considering the diagnosis of neuro-Behcet, since he patient reported recurrent ulcers in the oropharynx and folliculitis in his medical history, treatment with steroidal anti-inflammatory was initiated. Both the headache and the CSF changes remarkably improved. **Conclusion** an array of infectious agents can present as CM, but a nearly identical syndrome can result from a number of inflammatory, malignant, or other noninfectious diseases. **Key words:** chronic meningitis, neuro-Behcet

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CONSIDERATION ON A CASE OF HAEMORRHAGIC FEVER WITH RENAL SYNDROME

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We shall present the case of MI, male, aged 53, from Teasc/Dolj county, admitted in September 2014 with fever, jaundice, myalgias, epistaxis and diffuse petechiae. From the epidemiological point of view the patient worked as a farmer, he was recently gone for fishing (he was in contact with stagnant water) and he admitted to have mice in the household. Biological explorations revealed leukocytosis with lymphocytosis, monocytosis and plasmocytosis, trombocytopenia, increased total bilirubin level (mainly with the conjugate component), increased BUN and creatinine levels. We have suspected a case of leptospirosis and the patient started antimicrobial therapy with Ampicillin, 6g/day, i.v. Serological tests for leptospirosis, infectious mononucleosis, HIV infection and acute hepatitis A/B/C were negative. Medulogram showed an important percentage of plasmocytes (20%), while immunoelectrophoresis revealed increased IgM level, which raised the suspicion of multiple myeloma, but the hypothesis has been invalidated by a flowcytometry examination. Finally, the serology for hantaviruses was positive (IgM+ for Dobrava-Belgrade strain). **Discussion:** infections due to hantaviruses are less known / described in our country, however this infection should be suspected in cases of haemmorhagic fever with renal syndrome and negative serology for *Leptospira* spp. Haematologic features of this infection might also resemble the suspicion of lymphocytic leukaemia, multiple myeloma or heavy chain disease. **Conclusion:** in cases with epidemiological and clinical features suggestive for leptospirosis, but with negative serology it is recommended to search for hantavirus infection.**Keywords:** haemmorhagic fever with renal syndrome, hantavirosis, Dobrava-Belgrade strain

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VARICELLA ASSOCIATED WITH DEEP VEIN THROMBOSIS AND POSSIBLY PULMONARY INFARCTION IN A YOUNG PERSON WITH GENETIC RISK FACTORS

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In special hosts with predisposing risk factors, varicella might have surprising complications. We shall present the case pf the patient (Px) S.G., male, 37 years old, admitted in our hospital between 14 January to 01 March 2013. The onset of the disease was 10 days before admission, with fever and chills for about 4 days, followed by the appearance of the varicelliform rash and normalisation of the body temperature. After 3 more days fever and chills relapsed, and pain in the left ankle developed. 24 hours later pulmonary problems emerged (chest pain, cough, dyspnoea). He was admitted in our hospital with the following diagnoses : Left side pneumonia. Deep vein thrombosis. Chickenpox. On admission: fever; varicelliform rash (crusts), calor/tumor/dolor and positive Homans sign on the left ankle, dullness on the basal left side of the chest and reducing breath sounds. He had leukocytosis and neutrophilia, and the chest X ray showed diffuse opacity on the left side. Cardiologic examination: suspected pulmonary infarction; it requires anticoagulation. He was treated with Ceftriaxone, Ciprofloxacin and Sintrom and the evolution was slowly favourable. Genetic tests showed heterozigotism for factor V G1691A Leiden mutation. **Conclusion:** coagulopathy due to genetic predisposition lading to deep vein thrombosis and pulmonary infarction, highlighted by varicella-zoster infection. **Keywords:** varicella, deep vein thrombosis, pulmonary infarction, factor V Leiden.

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PLASMODIUM FALCIPARUM MALARIA IN A ROMANIAN TOURIST RETURNING FROM ENDEMIC AREA FOR EBOLA

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In Romania, malaria represent the main imported disease in patients returning from Africa. Since march 2014 countries of West Africa faced with the largest epidemic haemorrhagic fever caused by an Arbovirus - Ebola virus. The first confirmed case of Ebola in Nigeria, was at the end of July, in a patient returning from Liberia, initially suspected to have malaria. In 10 August 2014, a 51 years male romanian patient, returned from Nigeria in 25 July, without antimalarial chemoprophylaxis, is admitted in Intensive Care Unit of "Dr. Victor Babes" Clinical Hospital of Infectious and Tropical Diseases – Bucharest, complaining for fever, malaise, haemorrhagic diarrhea and food, followed by bloody vomiting. The onset was 2 weeks before, with significant worsening in the last 5 days. Malaria rapid test was positive for Plasmodium falciparum, then and thin and thick smears were positive for Plasmodium falciparum malaria, with multiple severity criteria (confusional syndrome – impaired consciousness, prostration, jaundice, 13% parasitemia, anemia, acute kidney injury, metabolic acidosis). The patient is also diagnosed with enterohaemorrhagic Escherichia coli O157 strain enterocolitis. We started right away antimalarial treatment with Artesunate and Clindamycin, with favorable outcome and restitutio ad integrum after 16 days of hospitalization. Epidemiolologic West African context required rapid differential diagnosis between infection with Ebola virus and malaria. Malaria can be a fatal disease in the absence / delay of the etiologic antiparasitic treatment, presenting this case, revealing the importance of both positive rapid diagnosis of malaria, as well as the establishment of early specific treatment.

Keywords: severe malaria, *Plasmodium falciparum*, Artesunate

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LONG-TERM FEVER SYNDROME – ETIOLOGY, DIAGNOSIS AND TREATMENT

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Introduction: long-term fever syndrome needs a complex approach in terms of clinic and laboratory and has social-economical implications regarding hospitalization costs and professional absenteeism. **Objective**: etiological assessment, clinical particularities and therapeutic approach. **Material and method**: the study presents the results of a retrospective study on 53 adult cases hospitalized at Bucharest 'Victor Babes' Infectious and Tropical Diseases Clinic, between 2013 and 2014 for long term fever syndrome. **Results and discussion**: most prevalent in males (58.6%); the patients' ages were between 18 and 85 years old, with a median age of 45 years old. Distribution according to etiology: infectious 70% (sepsis, hepatic abscess, pulmonary, endocarditis, tuberculosis, Q fever, CMV infection), neoplastic 15% (lymphoma, leukemia, hepatic cancer), autoimmune disease 7.5% (*collagenosis*, thyroiditis, rheumatic polyarthritis), unclassified 7.5%. **Conclusions**: for a correct diagnosis, patient history, laboratory investigations, interdisciplinary consults and/or therapeutic tests are essential. Etiologic diagnosis was established in 92% of cases, the most common etiology being infectious (70%). A large spectrum antibiotic therapy is the preferred first alternative until a concrete diagnosis is confirmed. **Keywords:** long-term fever syndrome, etiology, therapy

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FAVORABLE EVOLUTION OF A RECURRENT STAPHYLOCOCCUS INFECTION LOCATED ANTERIOR THORACIC (PECTORALLY LEFT) UNDER CEFTAROLIN TREATMENT, AS A RESULT OF IMPLANT OF A LEFT VENTRICULAR HEARTWARE VAD ASSISTING DEVICE

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 DOI: 10.12865/CHSJ.42.03.12

Male , 53 years old , Botosani County, is admitted in Clinical Hospital of Infectious Diseases "Sf.Parascheva" Iasi on 18.05.2014 for : fever , chills , drowsiness , swelling , pain, in the context of a purulent collection located on the left hemithorax (pectoral area). From the personal pathological history we remarked : complicated miocarditis with dilated cardiomyopathy and acute pulmonary oedema , necessiting implant of a left ventricular VAD type Heartware assisting device (cardiac pretransplant surveillance mode) a month before + July 2013 and January 2014 Sepsis with Methicillin-resistant staphylococcus (treated with Vancomicin / Linezolid + Ciprofloxacin) .Purulent collection reappeared in the left anterior hemithorax area in April 2014 followed by short term remission (under treatment with Vancomicin and Ciprofloxacin in Botosani) followed by relapse of the purulent collection exteriorized with a fistula , in which was isolated Methicillin-resistant staphylococcus(in our hospital). At addmitance, general estate was moderately influenced ,revealing a subcutaneous collection on the left pectoral area ,detecting a sistolic murmur gr. V-VI /6. pluriorificial , with maximum intensity in the II nd left intercostal space , TA: 92/70mm hg , FC 80 bpm ,painful abdomen in the left hypochondrium. Laboratory findings: WBC:14290/mm3 , NT:71% , ESR 40mm/1h . On 24.05.2014 was performed a soft part ecography of the left pectoral area, which revealed a inhomogenous subcutaneous collection of about 44mm/33mm , relatively well delimited,with extension under costal plan .Purulent liquid from the collection isolated Methicillin-resistant staphylococcus sensible at Vancomicin , Linezolid and Ceftaroline (also Biseptol and Aztreonam). Collection interested only soft parts, with no cardiac involvment. (Ecocardiography was normal). Pacient received treatment with Zinforo (Ceftaroline) 1,2g/zi i.v for 14 days , therapeutical option considered to be of choice in accordance with the anterior therapies with Vancomicin and Linezolid. Evolution was favorable with complete remission of the general and local symptoms ,without other subjective complains from the patient followed by improvment of the biological findings (WBC 6520/mm3, NT 58,2% , VSH 20mm/1h), clinical and biological state of the patient remaining unmodified next 2 weeks after release. **Discutions and Conclusions**: in vitro studies show that Ceftaroline has bactericid effect and is capable to inhibit the bacterial wall synthesis of methicillin-resistant Staphylococcus aureus (SAMR)due to the high affinity for penicillin-binding proteins (PBP) which is found in some microorganisms. Zinforo has a superior effect comparing to other 3-4 generation cephalosporins or other antibiotics known to have antistaphylococcal activity. Zinforo is indicated for the treatment of complicated skin and soft tissue infections and community-acquired pneumonia,being a right choice even in reccurent infections due to sensitive germs. **Key words** : pectoral purulent collection , Methicillin-resistant staphylococcus , Ceftaroline

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MULTIDISCIPLINARY APPROACH TO LATE PRESENTER HIV PATIENT WITH MULTIPLE CO-MORBIDITIES – THE KEY OF THERAPEUTIC SUCCESS

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Introduction: HIV-positive patients with multiple co-morbidities require a multidisciplinary approach. The patient of 36 years, was admitted to our emergency service 14.05.2014, the 14th day of sickness : headache, asthenia, confusion syndrome, balance disorder, fever. Multiplanar cranial MRI examination revealed multiple brain abscesses (8) with perilesional edema. The ELISA, Western blot test confirmed HIV infection, CD4 lymphocyte: 26/µl. Sputum was positive for acid fast bacilli in June. Examination of cerebrospinal fluid: clear, 140 lymphocytes/mm^3, glucose: 20mg/dl, proteins: 140mg/dl, yeast cells, positive for cryptococcal antigen. Antiretroviral (Viread, Emtriva, Isentress), antifungal, anti-tuberculosis, PCP prophylaxis theraoy was initiated. In July: fever, herpes zoster, pneumococcal pneumonia develop. Chest CT scan, bronchoscopy, surgical consult, raise the suspicion of stenosing infiltrative, proliferative, lung process and pleura invasion. Negative histopathology, negative tumor markers (CYFRA 21-1, SCC) had disproved the diagnosis. In October CD4 lymphocytes: 90/µl. In December cranial CT reveals seven calcified lesions and two still active, CT chest without elements suggestive of tumoral process. In January 2015

electroneurographic examination reveals axonal polyneuropathy. Currently, HIV seropositive patient, C3 state, sensorimotor neuropathy associated to infections and drug reactions, state after cerebral toxoplasmosis, cryptococcal meningoencephalitis, pulmonary tuberculosis, with very good adherence to complex treatment, perhaps, with a syndrome of immunological reconstruction syndrome in July. **Conclusions**: multidisciplinary management, therapeutic consistency, thorough differential diagnosis, patient adherence to complex treatment, defined the key of success in our case. **Keywords**: HIV, late presenter, comorbidities, treatment
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ANTIMICROBIAN PEPTIDES AND BACTERIOPHAGES: ALTERNATE AND / OR COMPLEMENTARY TREATMENT OF INFECTIONS

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Prolonged use of antibiotics - sometimes irrational - resulted in microbial resistance gaining; at present, some bacteria are resistant to all known antibiotics. Therefore efforts are being made worldwide to discover new antibiotics and / or improving existing ones.

Antimicrobial peptides emerged as a new class of antimicrobials. The peptides are low molecular weight proteins consisting of a few amino acids. These are important components of the innate immune system of each body. Some have proven antibacterial activity of gram positive and negative. Their mechanism of action is the disruption of the cell membrane, followed by the formation of pores and the permeability of the membrane. The main families are: Megainine, Chatilecidine, defensins. There are synthetic preparations: Pexiganan, Plectasin, Brilacidin, Litixar.

Phage therapy ,heavily used before the advent of antibiotics, currently reemerged. Experiments on animals have shown promising results in lung infections with *Pseudomonas* spp. Phage therapy is more targeted than antibiotics because it is addressed strictly pathogens identified. In cases of unidentified bacteria a cocktail composed of several bacteriophages can be used, based on the presumed etiological criteria. Phage therapy gave promising results in the treatment of MRSA skin infections, chronic skin ulcers and burns infected with *Pseudomonas* spp..

Phage therapy may be administered both orally and topically (spray).

Both peptides and phage therapy can be used alternative and complementary.

 DOI: 10.12865/CHSJ.42.03.12